ESSENTIALS OF HISTOLOGY.

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HISTOLOGY

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DIRECTIONS FOR CLASS WORK IN PRACTICAL PHYSIOLOGY:

Elementary Physiology of Muscle and Nerve and of the Vascular and Nervous Systems.

LONDON: LONGMANS, GREEN, & CO.

A COURSE OF PRACTICAL HISTOLOGY,

Containing plain directions for individual work in Histology.

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A TEXT-BOOK OF PHYSIOLOGY FOR ADVANCED STUDENTS.

BY BRITISH AUTHORS.

EDITED BY E. A. SCHÄFER, F.R.S.

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THE ESSENTIALS

OF

HISTOLOGY

DESCRIPTIVE AND PRACTICAL

FOR THE USE OF STUDENTS

BY

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PREFACE

This Book is written with the object of supplying the student with directions for the microscopical examination of the tissues. At the same time it is intended to serve as an Elementary Text-book of Histology; comprising the essential facts of the science, but omitting less important details.

For conveniently accompanying the work of a class of medical students, the book is divided into fifty lessons. Each of these may be supposed to occupy from one to three hours, according to the relative extent to which the preparations are made beforehand by the teacher, or during the lesson by the students. A few of the preparations cannot well be made in a class, but it has been thought advisable not to injure the completeness of the work by omitting mention of them.

Only those methods are recommended upon which experience has proved that dependence can be placed, and the directions given are for the most part capable of ready modification in accordance with the ideas or experience of different teachers.

CONTENTS.

INTRODUCTORY.

PAGE

Enumeration of the Tissues—General Structure of Animal Cells—Division of Cells, - - - - - - - - 1

LESSON I.

Use of the Microscope—Examination of Common Objects, - - 26

LESSONS II. and III.

Human Blood-Corpuscles—Development of Blood-Corpuscles—Bone-Marrow. - - - - - - - - - - - 30

LESSON IV.

Action of Reagents upon the Human Blood-Corpuscles. - - - 48

LESSON V.

Blood-Corpuscles of Amphibia, - - - - - - - - 52

LESSON VI.

Amœboid Phenomena of the Colourless Blood-Corpuscles. - - 57

LESSON VII.

Epithelium and Secreting Glands, - - - - - - - 63

LESSON VIII.

PAGE
COLUMNAR AND CILIATED EPITHELIUM, - - - - - - - 72

LESSON IX.

CONNECTIVE TISSUES: AREOLAR AND ADIPOSE TISSUE—RETIFORM AND LYMPHOID TISSUE, - - - - - - - - - - 80

LESSON X.

CONNECTIVE TISSUES (*continued*): ELASTIC TISSUE—FIBROUS TISSUE—DEVELOPMENT OF CONNECTIVE TISSUE, - - - - - - 94

LESSON XI.

CONNECTIVE TISSUES (*continued*): ARTICULAR CARTILAGE—SYNOVIAL MEMBRANES, - - - - - - - - - - - 102

LESSON XII.

CONNECTIVE TISSUES (*continued*): COSTAL CARTILAGE—FIBRO-CARTILAGE, - - - - - - - - - - - - 108

LESSON XIII.

CONNECTIVE TISSUES (*continued*): STRUCTURE AND DEVELOPMENT OF BONE, - - - - - - - - - - 112

LESSON XIV.

STRIATED MUSCLE, - - - - - - - 128

LESSON XV.

CONNECTION OF MUSCLE WITH TENDON—BLOOD-VESSELS OF MUSCLE—CARDIAC MUSCLE—DEVELOPMENT OF MUSCLE—PLAIN MUSCLE, - 138

LESSON XVI.

NERVE-FIBRES, - - - 148

LESSONS XVII. AND XVIII.

PAGE

NERVE-CELLS—GANGLIA—DEGENERATION AND REGENERATION OF NERVE-FIBRES AND NERVE-CELLS—NEUROGLIA—DEVELOPMENT OF NERVE-CELLS AND NERVE-FIBRES, - - - - - - - - - - - 157

LESSON XIX.

MODES OF TERMINATION OF NERVE-FIBRES, - - - - - - - 188

LESSON XX.

THE LARGER BLOOD-VESSELS, - - - - - - - - - 208

LESSON XXI.

SMALLER BLOOD-VESSELS—LYMPH-VESSELS—MICROSCOPIC STUDY OF THE CIRCULATION—DEVELOPMENT OF BLOOD- AND LYMPH-VESSELS—SEROUS MEMBRANES, - - - - - - - - - - - - 216

LESSON XXII.

LYMPH-GLANDS—TONSIL—THYMUS, - - - - - - - - 232

LESSON XXIII.

SPLEEN—SUPRARENAL CAPSULES—THYROID BODY—CAROTID AND COCCYGEAL GLANDS—PITUITARY BODY, - - - - - - - 243

LESSONS XXIV. AND XXV.

SKIN, NAILS, HAIRS, ETC.—MAMMARY GLANDS, - - - - - 259

LESSON XXVI.

HEART, - - - - - - - - - - - - - 284

LESSON XXVII.

TRACHEA AND LUNGS, - - - - - - - - - - 290

LESSON XXVIII.

PAGE
Structure and Development of the Teeth, - - - - - 300

LESSON XXIX.

Tongue and Gustatory Organs—Mucous Membrane of the Mouth—Pharynx and Œsophagus, - - - - - - - - 312

LESSON XXX.

Salivary Glands, - - - - - - - - - - - 319

LESSON XXXI.

Stomach, - - - - - - - - - - - - - 326

LESSONS XXXII. AND XXXIII.

Small and Large Intestine, - - - - - - - - - 336

LESSONS XXXIV. AND XXXV.

Liver and Pancreas, - - - - - - - - - - 352

LESSON XXXVI.

Kidney, - - - - - - - - - - - - - 364

LESSON XXXVII.

Ureter, Bladder, and Male Generative Organs, - - - - 376

LESSON XXXVIII.

Generative Organs of the Female, - - - - - - 394

LESSONS XXXIX. AND XL.

Spinal Cord, - - - - - - - - - - - - 408

LESSON XLI.

PAGE
Medulla Oblongata, - - - - - - - - - - 428

LESSONS XLII. AND XLIII.

Pons, Mesencephalon, and Thalamencephalon, - - - - - 446

LESSONS XLIV. AND XLV.

Cerebellum and Cerebrum, - - - - - - - - - 474

LESSONS XLVI., XLVII., AND XLVIII.

Eye, - - - - - - - - - - - - - - 500

LESSON XLIX.

Olfactory Mucous Membrane—External and Middle Ear, - - 528

LESSON L.

Internal Ear, - - - - - - - - - - - - 533

APPENDIX.

Methods, - - - - - - - - - - - - 545

INDEX, - - - - - - - - - - - 563

THE ESSENTIALS OF HISTOLOGY.

INTRODUCTORY.

ENUMERATION OF THE TISSUES AND THE GENERAL STRUCTURE OF ANIMAL CELLS.

Animal Histology[1] is the science which treats of the minute structure of the tissues and organs of the animal body; it is studied with the aid of the microscope, and is therefore also termed *Microscopic Anatomy.*

Every part or organ of the body, when separated into minute fragments, or when examined in thin sections, is found to consist of certain textures or tissues, which differ in their arrangement in different organs, but each of which exhibits characteristic structural features.

The following is a list of the principal tissues which compose the body:—

1. **Epithelial.**
2. **Connective**: Areolar, Fibrous, Elastic, Reticular, Lymphoid, Adipose, Cartilage, Bone.
3. **Muscular**: Voluntary, Involuntary, smooth or plain, Cardiac.
4. **Nervous.**

Some organs are formed of several of the above tissues, others contain only one or two.

It is convenient to include such fluids as the *blood* and *lymph* amongst the tissues, because they are studied in the same manner and contain cellular elements similar to those met with in some of the other tissues.

All the tissues are, prior to differentiation, masses of *cells* (embryonic cells). In some tissues other tissue-elements become developed which take the form of *fibres.* Thus the epithelial tissues are composed throughout life entirely of cells, only slightly modified in structure, and the nervous and muscular tissues are formed of cells which are greatly modified to form the characteristic fibres of those tissues. On the other hand, in the connective tissues an amorphous material becomes formed between the cells which is termed *intercellular substance* or *ground substance*, and in this substance fibres make their appearance, sometimes, as in the fibrous connective tissues, in so large an amount as to occupy the whole of the intercellular substance, and greatly to preponderate over the cells. This ground substance, by virtue of its containing a certain amount of inorganic chlorides, has the property of becoming stained brown or black by nitrate of silver and subsequent exposure to light, in which case the cells, which remain unstained, look like white spaces (cell-spaces) in the ground substance. When an epithelial tissue is similarly treated, the narrow interstices between the cells are also stained, from which it may be concluded that a similar substance exists in small amount between the cells of this tissue. It has here been termed cement-substance, but it is better to apply to it the general term *intercellular substance.*

---

[1] From *ιστός* a web or texture.

The cells of a tissue are not always separate from one another, but are in many cases connected by bridges of the cell-substance, which pass across the intercellular spaces. This is especially the case with the cells of the higher plants, but it has also been found to occur in animal tissues, as in some varieties of epithelium and in cardiac and plain muscular tissue. Occasionally the connection of the cells of a tissue is even closer, and lines of separation between them are almost or entirely absent. The term *syncytium* is given to any such united mass of cells.

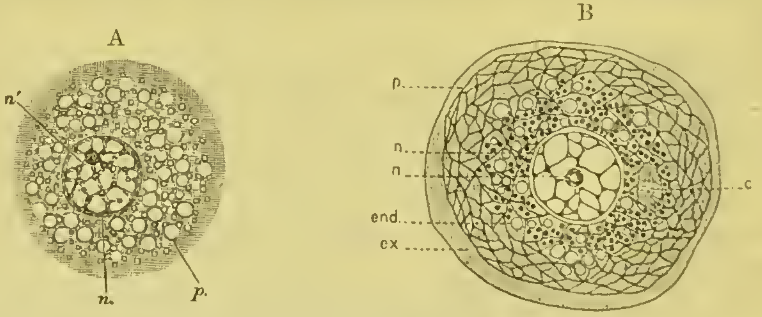


FIG. 1.—DIAGRAMS OF CELL-STRUCTURE.

A. Diagram of a cell the protoplasm of which appears structureless, but is occupied by vacuoles and granules.

B. Diagram of a cell the protoplasm of which appears reticulated.

p, protoplasm, consisting of hyaloplasm and a network of spongioplasm; *ex*, exoplasm: *end*, endoplasm, with distinct granules and vacuoles; *c*, double centrosome; *n*. nucleus; *n'*, nucleolus.

Cells.—A cell is a minute portion of living substance (*cytoplasm*) which is sometimes inclosed by a *cell-membrane* and always contains a specially differentiated part which is known as the *nucleus.*

The **cytoplasm** of a cell (fig. 1, *p*) is composed of *protoplasm*, which consists chemically of proteid or nucleoproteid substances, with which lipoid substances, such as *lecithin*, a combination of fatty acid with glycerophosphoric acid, and *cholesterin*, a monatomic alcohol, having many of the physical characters of fats, appear always to be associated. The protoplasm tends during life to exhibit movements which are apparently spontaneous, and when the cell is uninclosed by a membrane, a change in the shape, or even in the position of the cell, may be thereby produced. This is characteristically shown in the movements of the unicellular organism known as the amœba (fig. 2); hence the name *amœboid movement*, by which it is generally designated.[1] The protoplasm often, but not always, contains a fine spongework, which takes under high powers of the microscope the appearance of a network (figs. 3, 4), the remainder of the protoplasm being a clear substance which occupies the interstices of the sponge, and may also cover the surface or project beyond the rest of the cell. A granular appearance is often produced by the knots in the network when imperfectly observed looking like separate granules. The

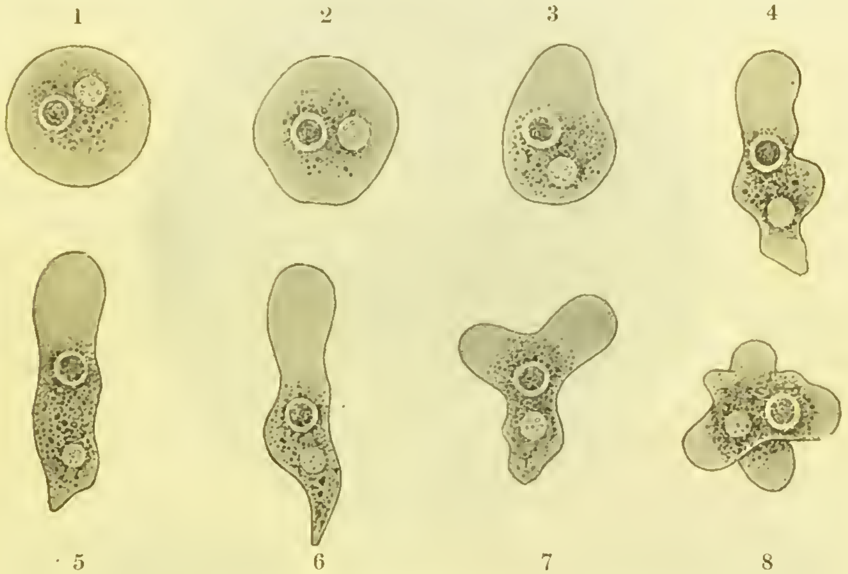


FIG. 2.—SUCCESSIVE CHANGES EXHIBITED BY AN AMŒBA. (Verworn.)

---

[1] The amœboid phenomena of cells will be studied later (in the colourless corpuscles of blood).

material which forms the reticulum is termed *spongioplasm*; the clearer material which occupies its meshes is *hyaloplasm*. The protoplasm of some cells shows a considerable degree of differentiation into fibrils, which may be unbranched or may form a network within the cell. Some cells exhibit a fine canalisation of their protoplasm (fig. 5), and according to Holmgren the canaliculi are in many cases occupied by branching processes of other (nutrient) cells, which form what he has termed a "trophospongium."

Protoplasm often, if not always, includes actual granules of a proteid nature (fig. 6). The granules are of several kinds. One kind stains with alkaline dyes (*basiphil*), another with acid dyes (*oxyphil*), others with basic and acid dyes (*amphophil*), and others with neutral dyes (*neutrophil*). Some of these granules may be essential constituents of the protoplasm (Altmann); others are materials which have been formed by the protoplasm, and which are in a sense accidental inclusions. That the former are of importance appears to be evident from the fact that many of the chemical changes of cells occur in them. Moreover, they are closely associated with the most active part of the protoplasm, the part, namely, in the neighbourhood of the nucleus, and appear to become formed in this part, and from it to extend through the cell. When fibrils

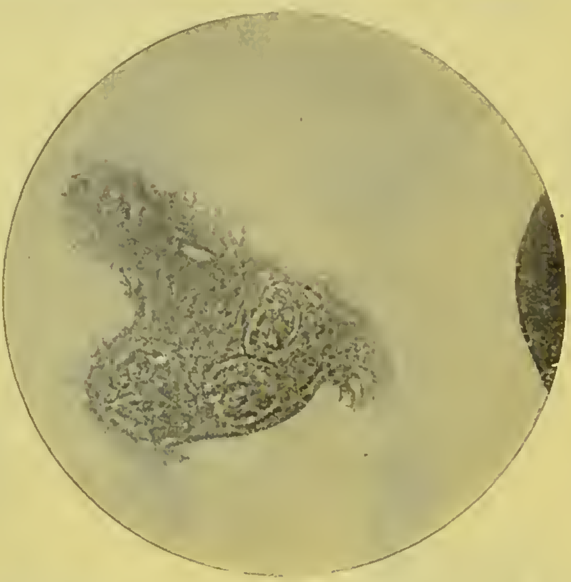


Fig. 3.—Untouched photograph of living leucocyte of triton, showing reticular structure of the protoplasm. (Schäfer.) Magnified 1360 diameters.

The photograph was taken in monochromatic light with Zeiss' 2 mm. apochromatic objective and projective eye-piece. The polymorph nucleus also exhibits the reticular structure.

are formed in the protoplasm, they are believed to be produced from the granules in question, to which the name *mitochondria* has

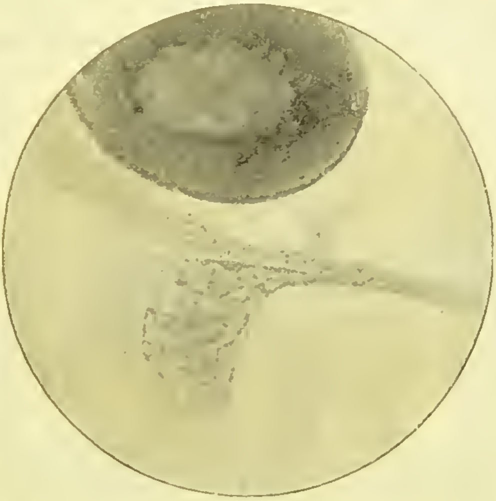


FIG. 4.—A LIVING LEUCOCYTE (WHITE BLOOD-CORPUSCLE) OF SALAMANDRA MACULATA, SHOWING LACE-LIKE RETICULAR APPEARANCE OF ITS PROTOPLASM. Magnified 1200 diameters.

An erythrocyte (red blood-corpuscle) is included in the photograph. A film of the protoplasm of the leucocyte extends over the margin.

been given (Benda), (fig. 7). The mitochondria are sometimes collected into a spherical mass near the nucleus which stains more deeply than the rest of the cytoplasm (fig. 8). To this body the term *paranucleus* has been applied. The granules referred to may

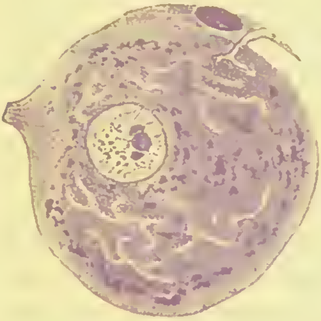


FIG. 5.—TROPHOSPONGIUM (CANALISATION) WITHIN A GANGLION CELL. (E. Holmgren.)

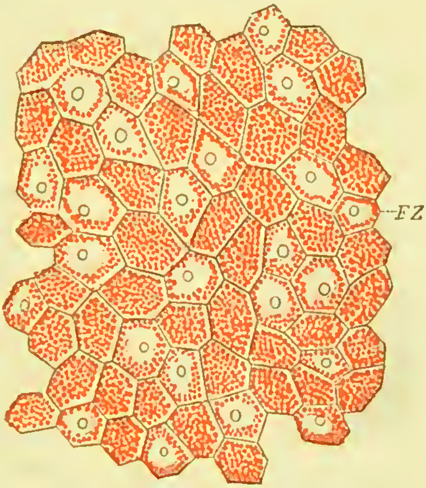


FIG. 6.—EPITHELIUM-CELLS OF SALAMANDER LARVA, STAINED *intra vitam* WITH NEUTRAL RED, SHOWING THE CELL-GRANULES. (Fischel.) Magnified 300 diameters.

be regarded as actual constituents of the cytoplasm, and formed directly from its protoplasm. As indicating this close connection with protoplasm they may conveniently be termed *deuteroplasm.* This name has also been used to include materials which are merely

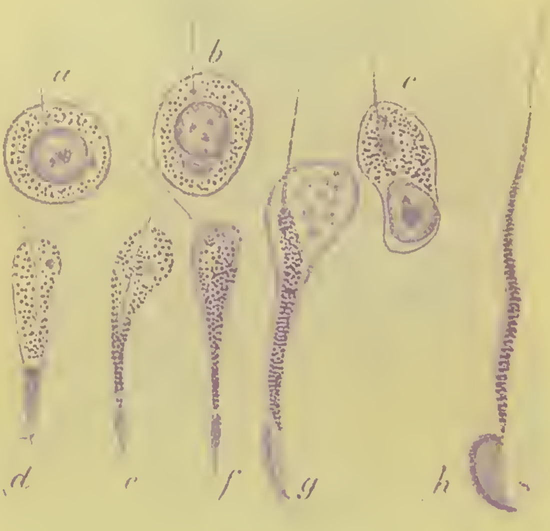


Fig. 7.—Cells from the testicle of the mouse in process of transformation into spermatozoa. (Benda.)

The "mitochondria" are darkly stained and are seen in the successive stages (*a* to *g*) to be arranging themselves so as to constitute the spiral filament of the spermatozoon (*h*).

included in the cytoplasm and not factors in its constitution, such as pigment granules, fat globules, and vacuoles containing watery fluid, with or without glycogen or other substances in solution. Materials which are thus included in the protoplasm of a cell are either stored up for the nutrition of the cell itself, or are converted into substances which are eventually extruded from the cell in order to serve some purpose useful to the whole organism, or to be got rid of from the body. The term *paraplasm* may be employed to denote any such materials within a cell. Paraplasm is often present in sufficient quantity to reduce the cytoplasm to a relatively small amount, the bulk of the cell being occupied by other material, as when starch becomes collected within vegetable cells or fat within

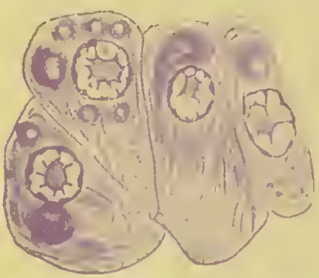


Fig. 8.—Pancreas cells of frog, showing paranucleus and chondromitome fibrils formed from mitochondria. (Gurwitsch, after Matthews.)

the cells of adipose tissue. It is frequently the case that the paraplasm and deuteroplasm are confined mainly to the middle of the cell in the neighbourhood of the nucleus, an external zone of the protoplasm being left clear. The two portions of protoplasm which are thus somewhat imperfectly differentiated off from one another are termed respectively the *endoplasm* and the *exoplasm*. They are exhibited in the amœba (fig. 2), and also in the white blood-corpuscle (fig. 9).

According to the view advocated by Bütschli the apparent reticulum or spongioplasm of a cell is the optical effect of a soft honeycomb or froth-like structure: in other words, the meshes of the reticulum do not communicate with one another as in a sponge, but are closed cavities as in a honeycomb. Bütschli finds indications of the same alveolar structure in all cells, including nerve-fibres and muscle-fibres, and has devised experiments with drops of froth made up of a mixture of oil and alkaline carbonate or sugar solution, which, when examined in water under the microscope, imitate very closely not only the structural appearance (fig. 10) but even the so-called spontaneous or amœboid movements of actual protoplasm. It may be stated, however, that although it is a matter of difficulty to determine whether a microscopic reticulum is a spongework or a honeycomb, it is probable that neither structure is essential to living substance, for the outermost layer of the cell protoplasm, which is usually the most active in exhibiting movements, often shows no indication of such structure. And further, it has been shown by Hardy that a colloid solution such as that which exists in protoplasm may, under some circumstances, appear homogeneous and under others may separate out into two parts, one more solid the other more fluid, and after such separation may exhibit either a granular, a reticular, or a honeycomb structure, according to circumstances. Nor is a "froth" necessary for the imitation of amœboid movements, for similar movements, due to changes in surface tension, and brought about in a simple oil drop or in a drop of oil-clad albumen when brought in contact with solution of soap or of any alkali (Berthold, Quincke). A drop of any colloid solution containing

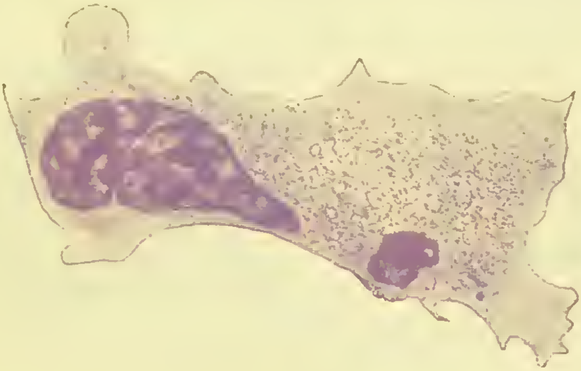


FIG. 9.—PHOTOGRAPH OF LEUCOCYTE OF TRITON, FIXED WHILST IN AMŒBOID CONDITION BY JET OF STEAM DIRECTED ON TO COVER-GLASS, STAINED WITH HÆMATOXYLIN. Magnified 1360 diameters. Untouched photograph. The protoplasm shows an internal granular and reticular endoplasm and a clear exoplasm.

electrolytes is also subject to such changes of surface tension when exposed to varying electrical influences, so that amœboid movements, which are certainly "vital," are capable of being explained by well-known physical laws.

There are grounds for believing that a very fine pellicle covers the exterior of the protoplasm of all free cells, and that this pellicle is composed of a material which, although not soluble in water, is permeable to watery fluids, and may also allow the passage of solids without rupture. Such a material might be furnished by the lipoids (Overton), which are, as we have seen, constant constituents of cell-protoplasm. It must, however, be stated that it has not been proved that these substances are collected at the surface of protoplasm.

Properties of living matter.—Living cells exhibit (1) *irritability* or the property of responding to stimuli ; (2) metabolie or chemical changes which result in *assimilation* or the taking in of nutrient matter and converting it into living substance (anabolism), and *disassimilation*, the property of breaking down or getting rid of such substance (katabolism) ; (3) *reproduction* resulting in the multiplication of cells. Of these properties (2) and (3) are certainly governed or influenced by the cell-nucleus, and (3) appears to be usually initiated by the centrosome (see below). The irritability of the cell depends, however, mainly upon the cytoplasm itself. It is in consequence of this property that protoplasm reacts, sometimes by contraction, sometimes by relaxation, to mechanical, chemical, thermal, and electrical stimuli, and in the case of some cells (*e.g.* the pigment-cells and cones of the retina) to the stimulus of light. The amœboid movements of cells are a manifestation of irritability, being produced and influenced by various external conditions and stimuli. Sometimes the result of a stimulus is to cause a cell or organism to move towards the source of excitation (attraction) ; in other cases the movement is in the reverse direction (repulsion). The terms positive and negative chemotaxis, phototaxis, thermotaxis, and the like, are used to indicate the nature of the effects produced by various forms of stimulation.

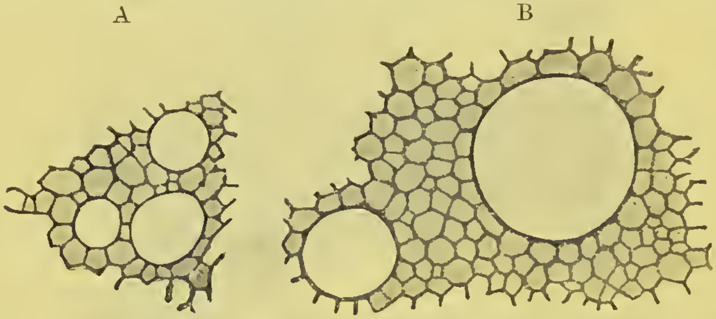


FIG. 10.—COMPARISON OF PROTOPLASM WITH OIL AND WATER EMULSION. (Verworn, after Bütschli.)

A. Protoplasm of Thalassicola.
B. Froth-like appearance of a mixture of oil and cane sugar.

Attraction-sphere and centrosome.—In some cells, as already indicated, there are fine but distinct striæ or fibrils (*cytomitome*) running in definite directions. These are very commonly met with in fixed cells, such as various kinds of epithelium-cells, nerve-cells, and muscle-cells. But besides these special differentiations, which appear to be related to special functions, there are other fibril-like structures in the

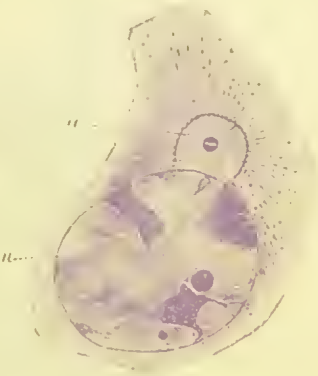


FIG. 11.—A CELL (WHITE BLOOD-CORPUSCLE) SHOWING ITS ATTRACTION-SPHERE. (M. Heidenhain.)

In this, as in most cases, the attraction-sphere, *a*, lies near the nucleus, *n*.

cell-protoplasm, associated with what is known as the *centrosome* (figs. 1, 9). This consists of a minute particle (*centriole*), usually situated near the nucleus, and staining darkly with iron-hæmatoxylin, surrounded by a clear area (*attraction-sphere*), and from it radiate into the surrounding protoplasm a number of fine varicose fibrils. The attraction-sphere, with its central particle, was first noticed in the ovum and was at first supposed to be peculiar to the egg-cell, but it has now been recognised in very many kinds of cells, and, in animal cells, is of nearly universal occurrence. The structures in question are frequently double, the twin spheres being connected by a spindle-shaped system of delicate fibrils (*achromatic spindle*): this duplication invariably precedes the division of a cell into two.

In some cells the centrioles are multiple; this is frequently the case with leucocytes and always with the giant-cells of bone marrow. The material which immediately surrounds the centrosome, and of which the radiating fibres and the fibres of the spindle are composed, is considered by some to be distinct in nature from the general protoplasm: it has been termed the *archoplasm*. It appears clear that in some cells the centrosome and archoplasm may have an existence independent of one another; thus no centrosome has been found in the cells of the higher plants, although the archoplasmic fibres are very well marked in them during cell-division.

A **cell-membrane** is rarely distinct in animal cells. When present, it is usually formed by transformation of the external layer of the protoplasm, but its chemical nature has not been sufficiently investigated. In plant cells a cellulose membrane is of common occurrence.

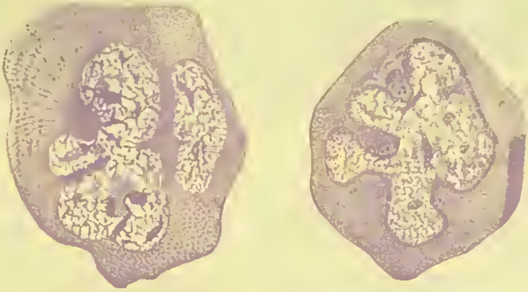


FIG. 12.—CELLS WITH IRREGULAR LOBED NUCLEI FROM BONE-MARROW OF RABBIT. (M. Heidenhain.)

The **nucleus** of the cell (fig. 1, *n*) is a small vesicle, spherical, ovoid, elongated, annular, or irregularly lobulated (figs. 11, 12, 13), embedded in the protoplasm. Cells have sometimes two nuclei, and occasionally several (fig. 13). The nucleus is bounded by a membrane which incloses a clear substance (*nuclear hyaloplasm, karyoplasm*) (fig. 14), and the whole of this substance is generally pervaded by an irregular network of fibres, some coarser, others finer (*nuclear reticulum, karyomitome*) (figs. 14, 15). The membrane is the outermost layer of the

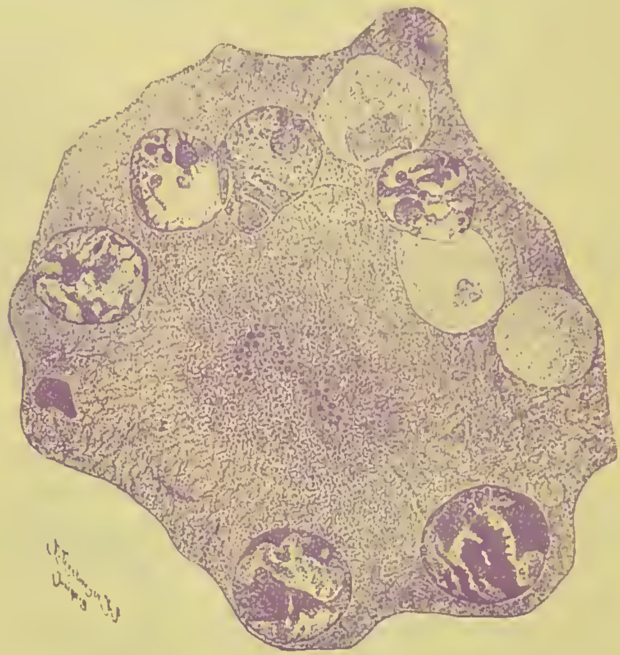


Fig. 13.—Multi-nucleated giant-cell from lymph gland of rabbit. (M. Heidenhain.)

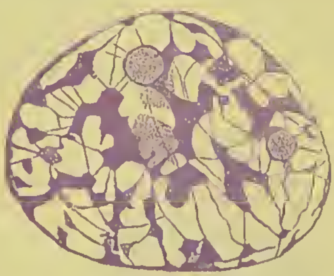


Fig. 14.—Nucleus of an epithelial cell of salamander larva. (M. Heidenhain.) Magnified 2300 diameters.

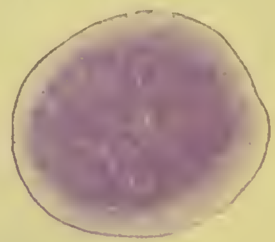


Fig. 15.—Lymphocyte of triton, showing the reticular structure of its nucleus. Magnified 2000 diameters. Untouched photograph.

The cell was fixed by steam, and afterwards stained with hæmatoxylin.

karyomitome. The knots of the nuclear reticulum are sometimes very distinct and give an appearance of conspicuous granules within the nucleus (*pseudonucleoli*), which are not to be confounded with the highly refracting spherical particle known as the **nucleolus**, which is generally present as a distinct structure. Sometimes two or more nucleoli are found (fig. 14). Occasionally the nucleolus has a vacuole-like globule in its interior. The material of the nucleolus, although basiphil, differs in its chemical and staining reactions from the nuclear reticulum. During cell-division it disappears. Whether it blends with karyomitome fibres or becomes absorbed and removed is at present uncertain. The nucleoli may sometimes be seen to be bodily extruded from the nucleus into the protoplasm. The nuclear membrane and intranuclear fibres stain deeply with haematoxylin and with basic dyes generally; this property distinguishes them from the nuclear matrix, and they are accordingly spoken of as *basi-chromatic* (containing *basi-chromatin*, which in the nucleus appears to be chemically identical with *nuclein*),

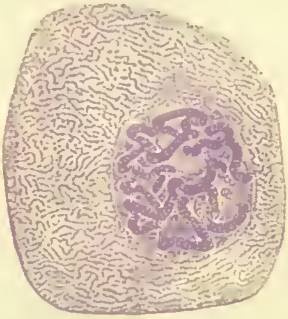


FIG. 16.—GLAND-CELL OF CHIRONOMUS. (Flemming.)

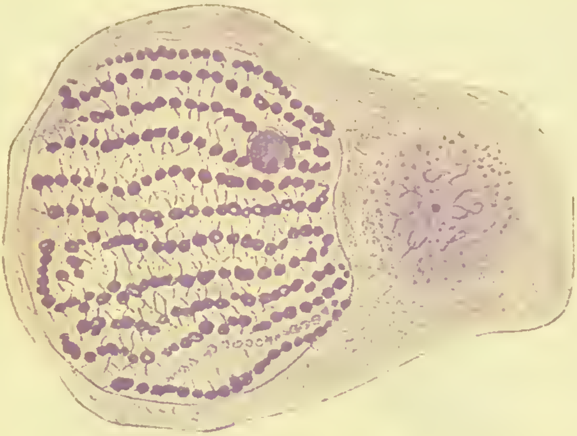


FIG. 17.—SPERMATOCYTE OF PROTEUS, SHOWING CHROMOSOMES OF NUCLEUS FORMED OF PARTICLES OF CHROMATIN UNITED BY ACHROMATIC FILAMENTS. (Gurwitsch, after Hermann.)

The nucleolus is distinct from the chromosomes. In the cytoplasm an archoplasmic mass containing mitochondria is seen on the right.

the hyaloplasm being *achromatic* or *oxychromatic*. The staining property depends upon the presence of minute basiphil or oxyphil granules. The basiphil granules are united by a non-staining material termed *linin*, into the threads or fibres which compose the network. Sometimes instead of being united into a network the intranuclear fibres take the form of convoluted filaments (*chromosomes*), having a skein-like arrangement (fig. 16). This is always found when a nucleus is about to divide, but it may also occur in the resting condition. These filaments may sometimes be seen with high magnification to be made up of fine juxtaposed particles (*chromomeres*) arranged either in single or double rows (figs. 17, 18,) which may impart a cross-striated appearance to the filament. The nuclear fibres are sometimes clumped together into a solid mass which comprehends the nucleolus when this is present, and has the appearance of an enlarged nucleolus. The fibres within the nucleus have been observed to undergo spontaneous changes of form and arrangement, but these become much more evident during its division. The division of the protoplasm is always preceded by that of the nucleus, and the nuclear fibres undergo during division a series of remarkable transformations which are known collectively by the term *karyokinesis* (Schleicher) or *mitosis* (Flemming). These changes may easily be studied in the division of epithelium cells, but exactly similar phenomena have been shown to occur in cells belonging to other tissues.

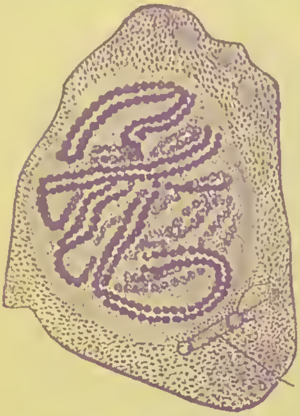


FIG. 18.—CELL SHOWING CHROMOSOMES OF NUCLEUS IN THE FORM OF THREADS COMPOSED OF DOUBLE ROWS OF CHROMOMERES. (F. Hermann.) *c*, centrosome with uniting spindle.

The simple division of a nucleus by a process of fission without karyokinetic changes is termed *amitotic division* (figs. 19, 20); it occurs in comparatively rare instances, and is not usually followed by the division of the cells, so that this is apt to result in the formation of bi-nucleated and multi-nucleated cells, as in the superficial layer of the epithelium of the urinary bladder and in some of the giant cells of bone-marrow.

The nucleus of the cell is not only concerned with its division and multiplication in the manner to be described, but takes an active part in the chemical (metabolic) processes which occur in the protoplasm. Hence cells deprived artificially of their nuclei do not assimilate nourishment, and lose any power of secretion they may have possessed, although the protoplasm may continue for a time to live and exhibit amœboid movements.

Division of cells.—The division of a cell is preceded by the division of its attraction sphere, and this again appears to determine the division of the nucleus. The latter, in dividing, passes through a series of remarkable changes, which may thus be briefly summarised as they occur in typical animal cells such as the epithelium cells of Salamandra:—

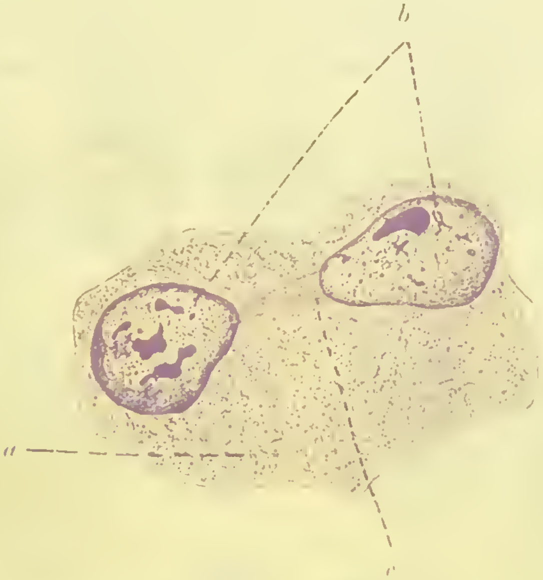


FIG. 19.—CELL OF BLADDER EPITHELIUM, SHOWING AMITOTIC DIVISION OF NUCLEUS. (Nemileff.)

a, cytoplasm; *b*, daughter nuclei; *c*, strand of fibrils uniting daughter nuclei.

1. The network of chromoplasm-filaments of the resting nucleus become transformed into a sort of *skein*, formed apparently of one long convoluted filament, but in reality consisting of a number of

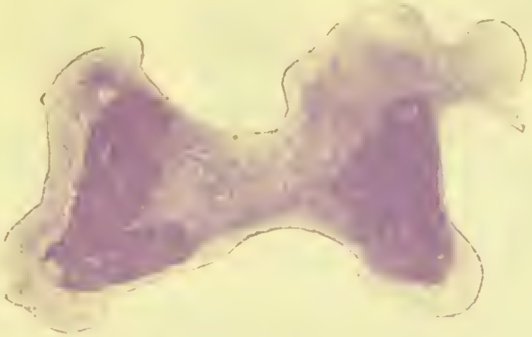


FIG. 20.—A LEUCOCYTE OF TRITON UNDERGOING AMITOTIC DIVISION. Magnified 1360 diameters. Untouched photograph.

The nucleus is separated into two nearly equal parts, and the protoplasm is collecting around them and becoming constricted in the intermediate part of the corpuscle. The corpuscle was fixed by a jet of a steam and stained with hæmatoxylin.

filaments (*spirem*); the nuclear membrane and the nucleoli disappear or are merged into the skein (fig. 21, *a* to *d*).

2. The filament breaks into a number of separate portions, often V-shaped, the *chromosomes*. The number of chromosomes varies with the species of animal or plant; in some animals the dividing nuclei may contain at this stage only four chromosomes; in man there are said to be twenty-four in the ordinary or somatic cells; a like number occurs in many animals and plants; others have more or fewer. As soon as the chromosomes become distinct they are often arranged radially around the equator of the nucleus like a star (*aster*, fig. 21, *e*, *f*, *g*).

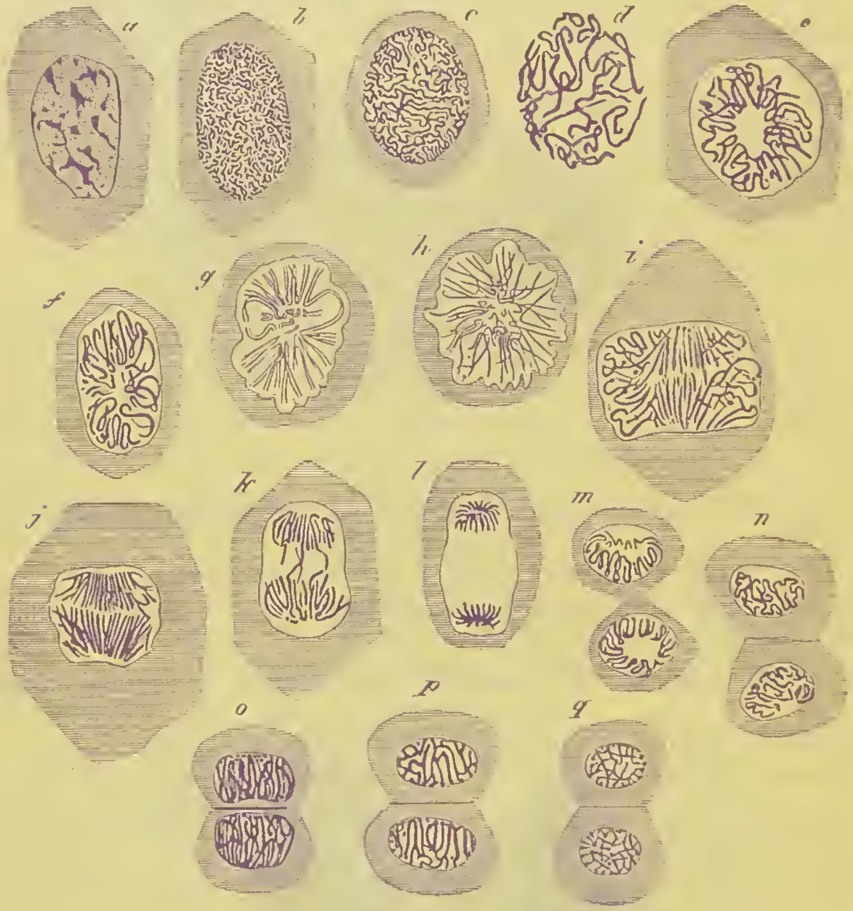


FIG. 21.—EPITHELIUM-CELLS OF SALAMANDER LARVA IN DIFFERENT PHASES OF DIVISION BY KARYOKINESIS OR MYTOSIS. (Flemming.)

3. Each of the chromosomes splits longitudinally into two, so that they are now twice as numerous as before (*stage of cleavage*,

fig. 21, *h*, *i*). This longitudinal cleavage may occur at an earlier stage.

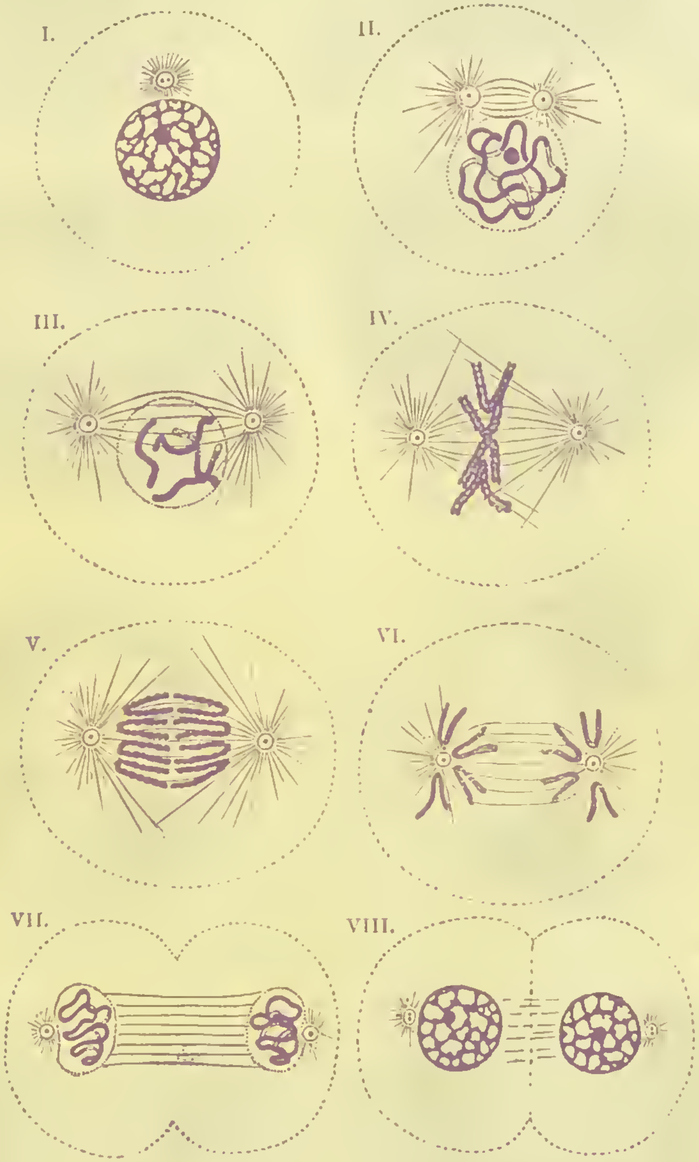


Fig. 22.—Diagram showing the changes which occur in the centrosomes and nucleus of a cell in the process of mitotic division. The nucleus is supposed to have four chromosomes.

4. The fibres separate into two groups, the ends being for a time interlocked (fig. 21, *j*, *k*).

5. The two groups pass to the opposite poles of the now elongated

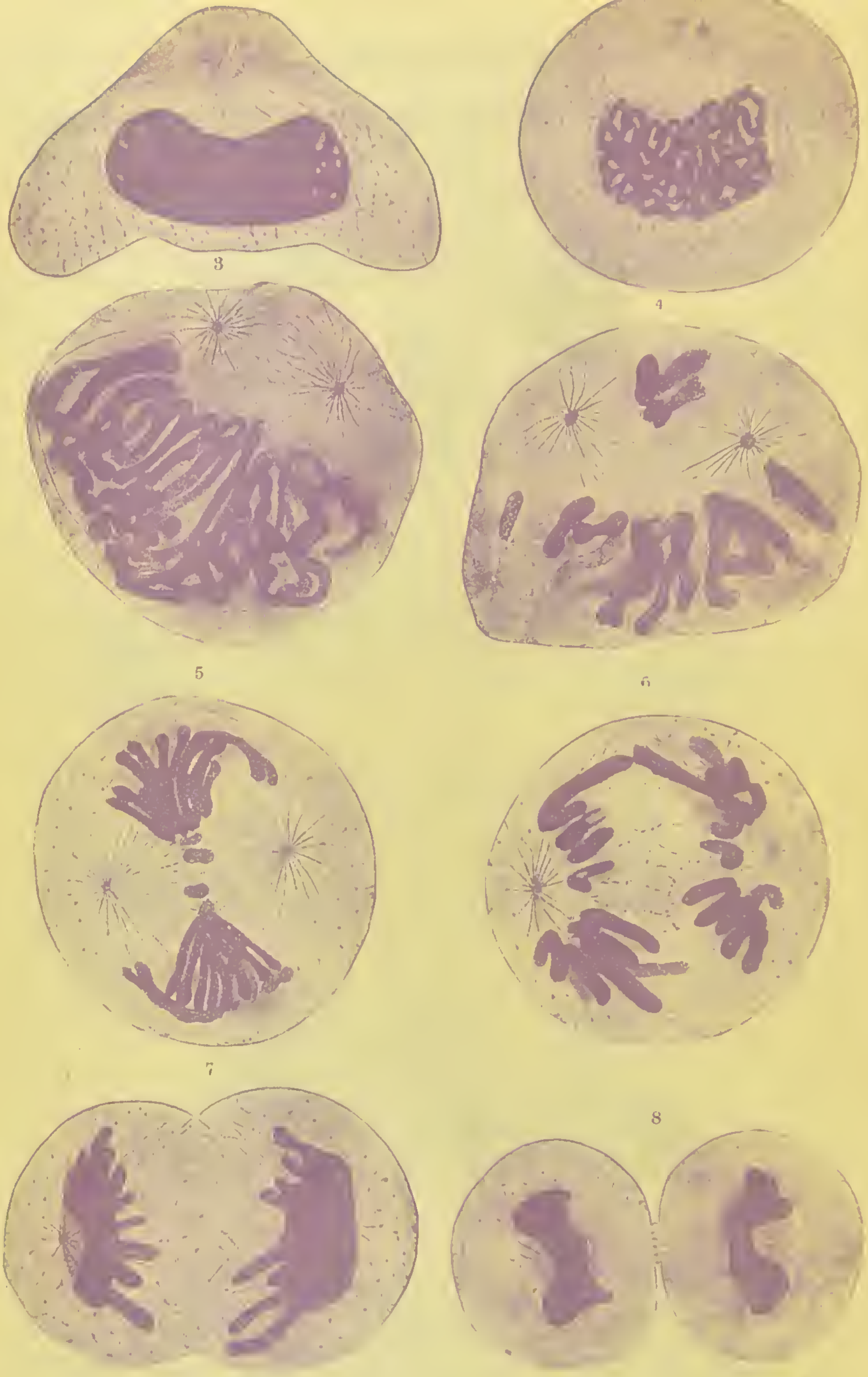


FIG. 23.—KARYOKINESIS OF ERYTHROCYTE OF LARVAL LEPIDOSIREN. (T. H. Bryce.)

1, Cell prior to division, centrosome single, nucleus a dense network; 2, centrosomes double, nucleus a close spirem; 3, spirem breaking up into chromosomes; division spindle forming, chromosomes V-shaped; 5, V-shaped chromosomes collected at equator of spindle, and undergoing longitudinal splitting; 6, the chromosomes which result from the splitting have become thicker and shorter, and are passing towards the centrosomes at the poles of the spindle to form the daughter nuclei; 7, 8, daughter nuclei formed by agglomeration of chromosomes, protoplasm of cell dividing.

nucleus and form a star-shaped figure at either pole (*diaster*, fig. 21 *l*), Each of the stars represents a daughter nucleus.

6, 7, 8. Each star of the diaster goes through the same changes as the original nucleus, but in the reverse order—viz., a skein, at first more open and rosette-like (fig. 21, *m*), then a closer skein (fig. 21, *n*), then a network (fig. 21, *o*, *p*, *q*); passing finally into the typical reticular condition of a resting nucleus (see also figs. 22, 23).

The splitting and separation of the chromosomes is often spoken of as the *metaphase* (*metakinesis*); the stages leading up to this being termed the *anaphase*, and those by which the process is terminated the *kataphase* and *telophase*.

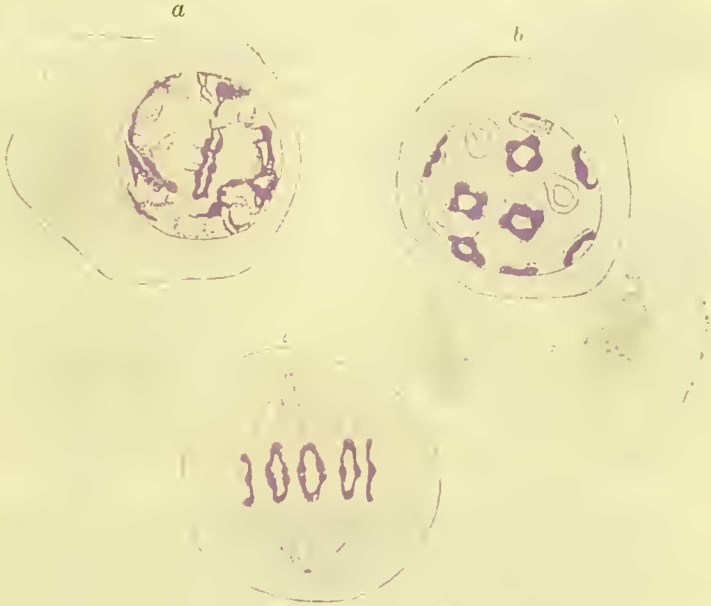


FIG. 24.—THREE STAGES OF HETEROTYPE MITOSIS IN SPERMATOCYTE OF TRITON. (Moore.)

a, geminal condition of chromosomes; *b*, gemini arranged in quadrate loops or tetrads; *c*, separation of tetrads into the duplex chromosomes of the daughter nuclei.

The mode of division of the nuclear chromatin above described is frequently spoken of as *somatic* or *ordinary mitosis*, to distinguish it from two modes of division which are only seen normally at certain stages of multiplication of the generative cells, and which are known as *heterotypical* and *homotypical mitosis*. In the latter the chromosomes do not undergo the usual longitudinal splitting, but one half of the total number passes into each daughter nucleus, so that the number of chromosomes in each of these is only one half the usual somatic number. This is termed the *reduction-division*. Heterotypical mitosis (which immediately precedes the homotypical) is characterised by a peculiar arrangement of the chromosomes, the split halves of which, before separating to pass to the daughter nuclei, tend to adhere together in the form of loops or rings, or in the case of short straight chromosomes into small quadrangular masses (tetrads), all of which are observable in various instances of heterotypical mitosis (see fig. 24).

It is further noteworthy that the generative cells which later undergo the reduction-division above described exhibit either immediately (sperm-cells) or a long while (germ-cells) before the final divisions a remarkable series of changes in their nuclear chromatin ; the chromosomes becoming first distinct in place of forming a network, then entangled together at one side of the nucleus (synaptic condition), and finally becoming again distinct, but now arranged in pairs (gemini) which later take various forms, such as double rods, loops, or rings as in heterotypical mitosis, but without forthwith proceeding to nuclear division.

The protoplasm of the cell divides soon after the formation of the diaster (fig. 21 *m*). During division fine lines are seen in the protoplasm radiating from the centrosomes at the poles of the nucleus, whilst other lines form a spindle of *achromatic* fibres within the nucleus, diverging from the poles towards the equator. These are usually less easily seen than the basichromatic fibres or chromosomes already described, but are not less important, for they are derived from the attraction-spheres. These, with their centrosomes, as we have seen, always initiate the division of the cell ; indeed they are often found divided in the apparently resting nucleus, the two particles being united by a small system of fibres forming a minute spindle at one side of the nucleus (fig. 1 B, *c*). When mitosis is about to take place this spindle enlarges, and as the changes in the chromatin of the nucleus which have been above described occur—which changes involve the disappearance of the nuclear membrane—the spindle gradually passes into the middle of the mitotic nucleus, with the two poles of the spindle at the poles of the nucleus, and with the fibres of the spindle therefore completely traversing the nucleus

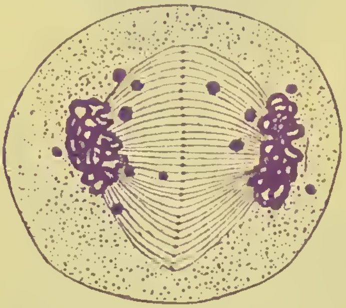


Fig. 25.—Cell-plate in dividing spore-cell of lily.
(Gurwitsch, after Zimmermann.)

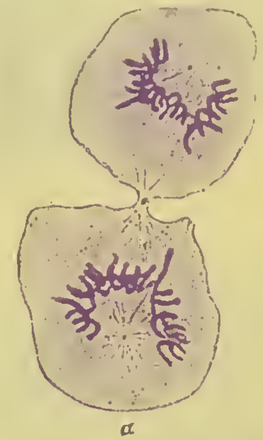


Fig. 26.—Dividing cell constricted to form two daughter cells each with centrosome. (Geberg.)
The particle at the junction of the daughter cells represents a rudimentary cell-plate.

(figs. 22, 23). The spindle-fibres appear to form directing lines, along which the chromosomes pass, after the cleavage, towards the nuclear poles to form the daughter nuclei.

In some cells, especially in plants, the line of division of the protoplasm of the cell becomes marked out by thickenings upon the fibres of the spindle which occur just in the plane of subsequent division, and have been termed collectively the *cell-plate* (fig. 25). But in most animal cells no cell-plate is formed, the protoplasm simply becoming constricted into two parts midway between the two daughter nuclei. Each daughter cell so formed retains one of the two attraction-particles of the spindle as its centrosome, and when the daughter cells are in their turn again about to divide this centrosome divides first and forms a new spindle, and the whole process goes on as before. Rarely the division of a nucleus is into three or more parts instead of two (fig. 27). In such cases the centrosome becomes correspondingly multiplied and the achromatic system of fibres takes a more complex form than the simple spindle.

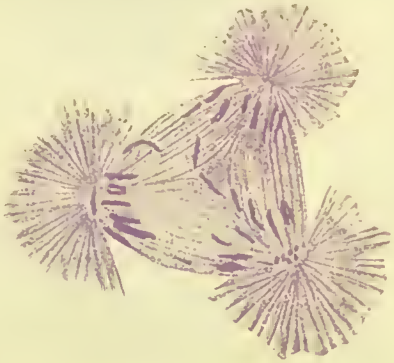


FIG. 27.—TRIPOLAR MITOSIS IN ECHINODERM OVUM. (E. B. Wilson.)

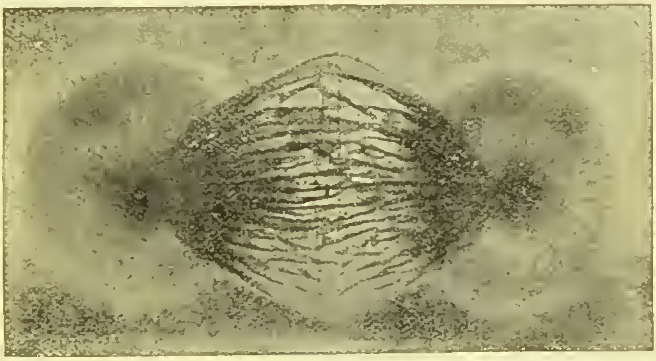
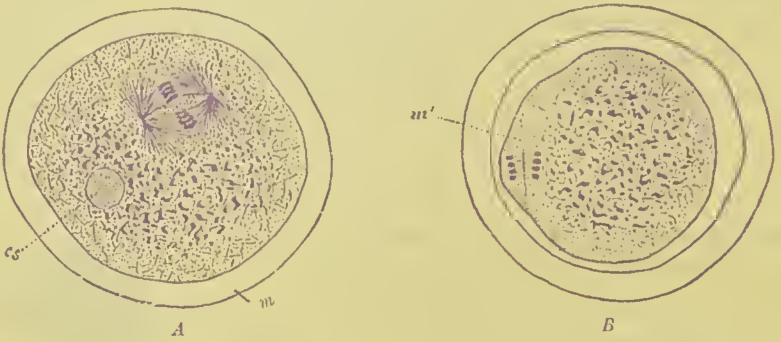


FIG. 28.—IMITATION OF DIVISION SPINDLE PRODUCED DURING THE MIXING OF DROPS OF A LESS CONCENTRATED SOLUTION OF AN ELECTROLYTE (CONTAINING PARTICLES OF CHINA INK IN SUSPENSION) WITH A SOLUTION OF THE SAME ELECTROLYTE OF GREATER DENSITY. (Verworn, after Leduc.)

The appearance of the division spindle and even the changes in the chromosomes can be imitated experimentally by introducing differences of electrical polarity in a solution of electrolytes containing particles in suspension (fig. 28). It is therefore not improbable that they are naturally brought about in some such manner.

Division of the ovum.—Usually the two daughter cells are of equal size; but there is a notable exception in the case of the ovum,



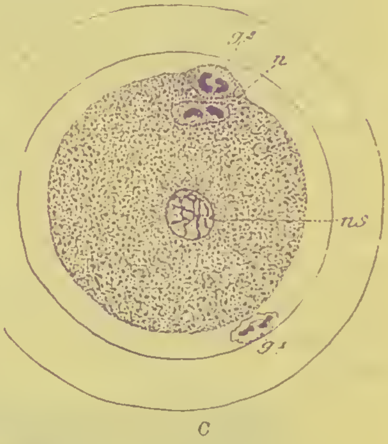


Fig. 29.—Formation of the polar globules and reduction of the number of chromosomes in the ovum of Ascaris megalocephala.

A, *B*, ovum showing division of nucleus to form first polar globule (Van Gehuchten). *m*, gelatinous envelope of ovum; *m'*, membrane dividing the polar globule from the ovum; *cs* (in *A*), head of spermatozoon.

C, formation of second polar globule (Carnoy); g^1, first; g^2, second polar globule: *n*, nucleus of ovum now containing only two chromosomes; *ns*, nucleus formed from head of spermatozoon.

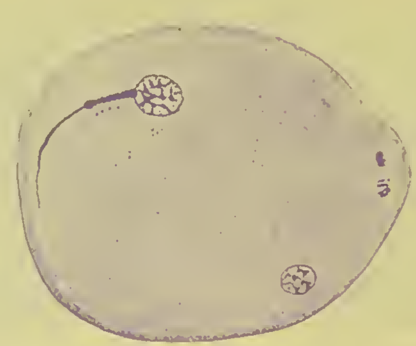


Fig. 30.—Ovum of bat with polar bodies and germ- and sperm-nuclei. (Van der Stricht.)

The development of the sperm-nucleus from the head of the spermatozoon is very evident in this case, because the rest of the spermatozoon happens not to have been thrown off.

which, prior to fertilisation, divides twice (by hetero- and homotypical mitosis respectively) into two very unequal parts, the larger of which retains the designation of ovum, while the two small parts which become detached from it are known as the *polar bodies* (fig. 29). Further, in the formation of the second polar body a *reduction-division*

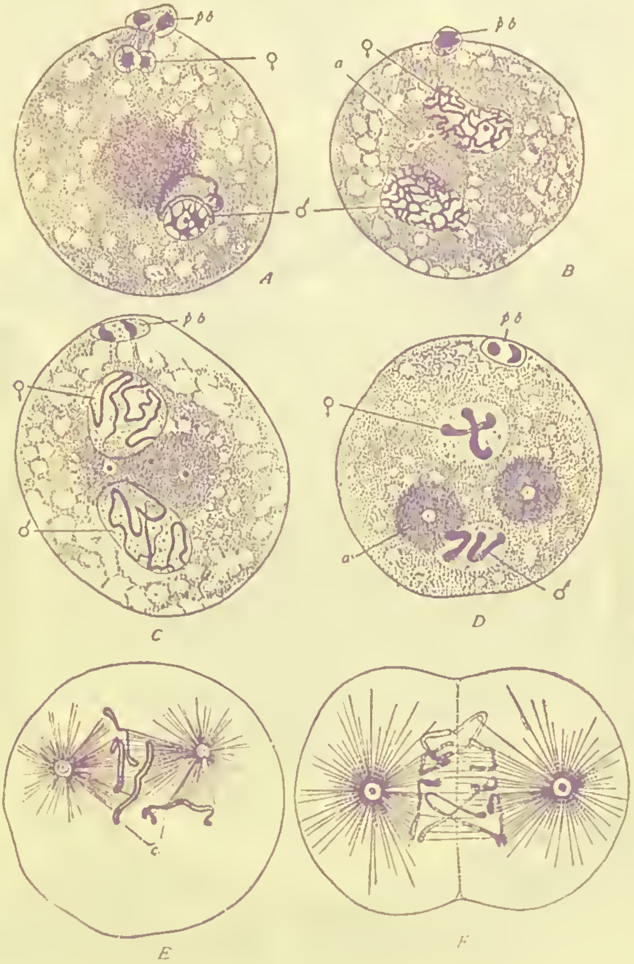


FIG. 31.—FERTILISATION AND FIRST DIVISION OF OVUM OF ASCARIS MEGALOCEPHALA (slightly modified from Boveri).

A, second polar globule just formed; the head of the spermatozoon is becoming changed into a reticular pro-nucleus (♂), which shows distinctly two chromosomes; just above it, its archoplasm is shown: the egg pro-nucleus (♀) also shows two chromosomes.

B, both pro-nuclei are now reticular and enlarged; a double centrosome (*a*) is visible in the archoplasm which lies between them.

C, the chromatin in each pro-nucleus is now converted into two filamentous chromosomes; the centrosomes are separating from one another.

D, the chromosomes are more distinct and shortened; the nuclear membranes have disappeared; the attraction-spheres are distinct.

E, mingling and splitting of the four chromosomes (*c*); the achromatic spindle is fully formed.

F, separation (towards the poles of the spindle) of the halves of the split chromosomes, and commencing division of the cytoplasm. Each of the daughter cells now has four chromosomes; two of these have been derived from the ovum pro-nucleus, two from the spermatozoon pro-nucleus.

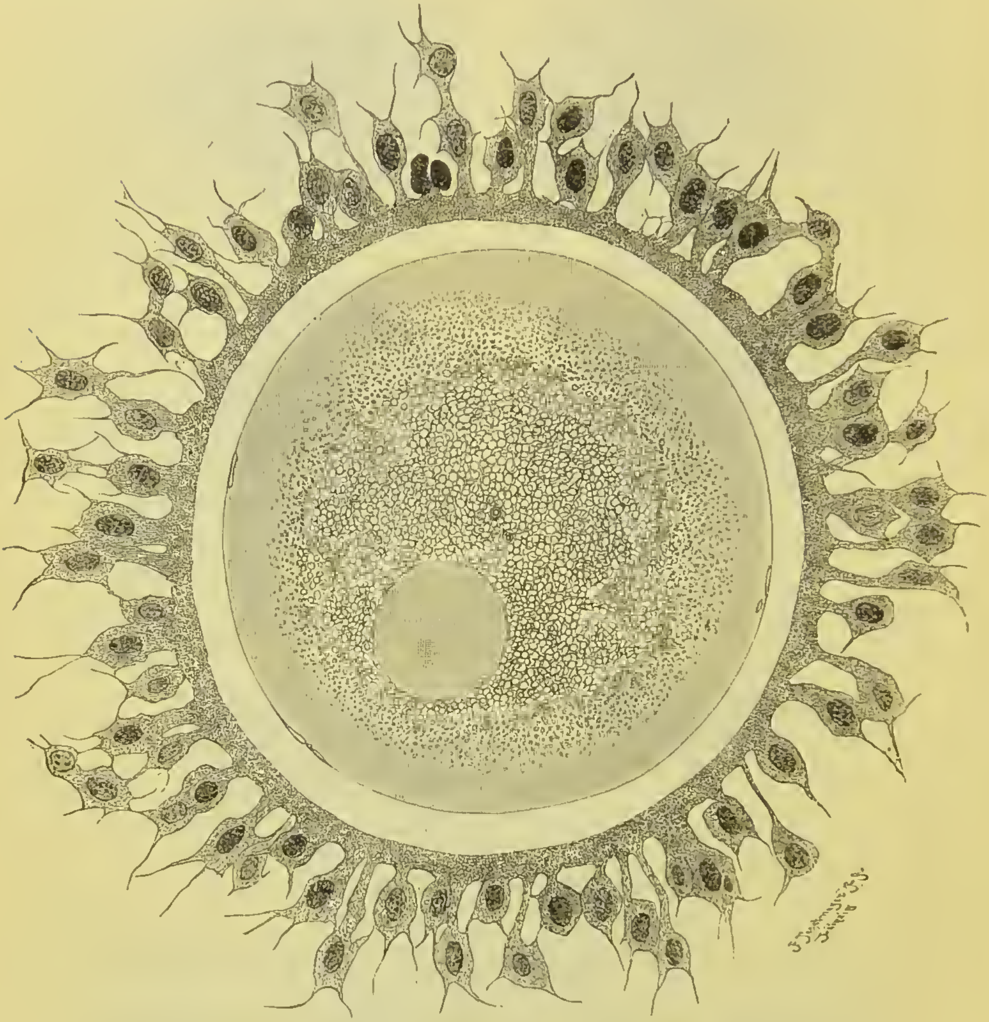


FIG. 32.—HUMAN OVUM (OOCYTE) FROM GRAAFIAN FOLLICLE: EXAMINED FRESH IN LIQUOR FOLLICULI WITH VERY HIGH MAGNIFYING POWER. (Waldeyer.)

The cells which are attached to the outside, and which appear to be joined into a syncytium around the ovum, are follicular cells belonging to the *discus proligerus*. Within them is the clear membrane of the ovum (zona pellucida). The cytoplasm of the ovum shows a distinction between clear ectoplasm and granular endoplasm: the large granules are yolk particles. The nucleus (germinal vesicle) is clear. The nucleolus (germinal spot) is distinct.

occurs, and the nucleus of the ovum, after the polar bodies are extruded, contains only one half the number of chromosomes that it had previously: *e.g.* twelve in place of the normal twenty-four in man, and two instead of four in Ascaris megalocephala (var. bivalens), (fig. 29, *C*). Should fertilisation supervene the chromosomes which are lacking are supplied by the male element (sperm-cell), the nucleus

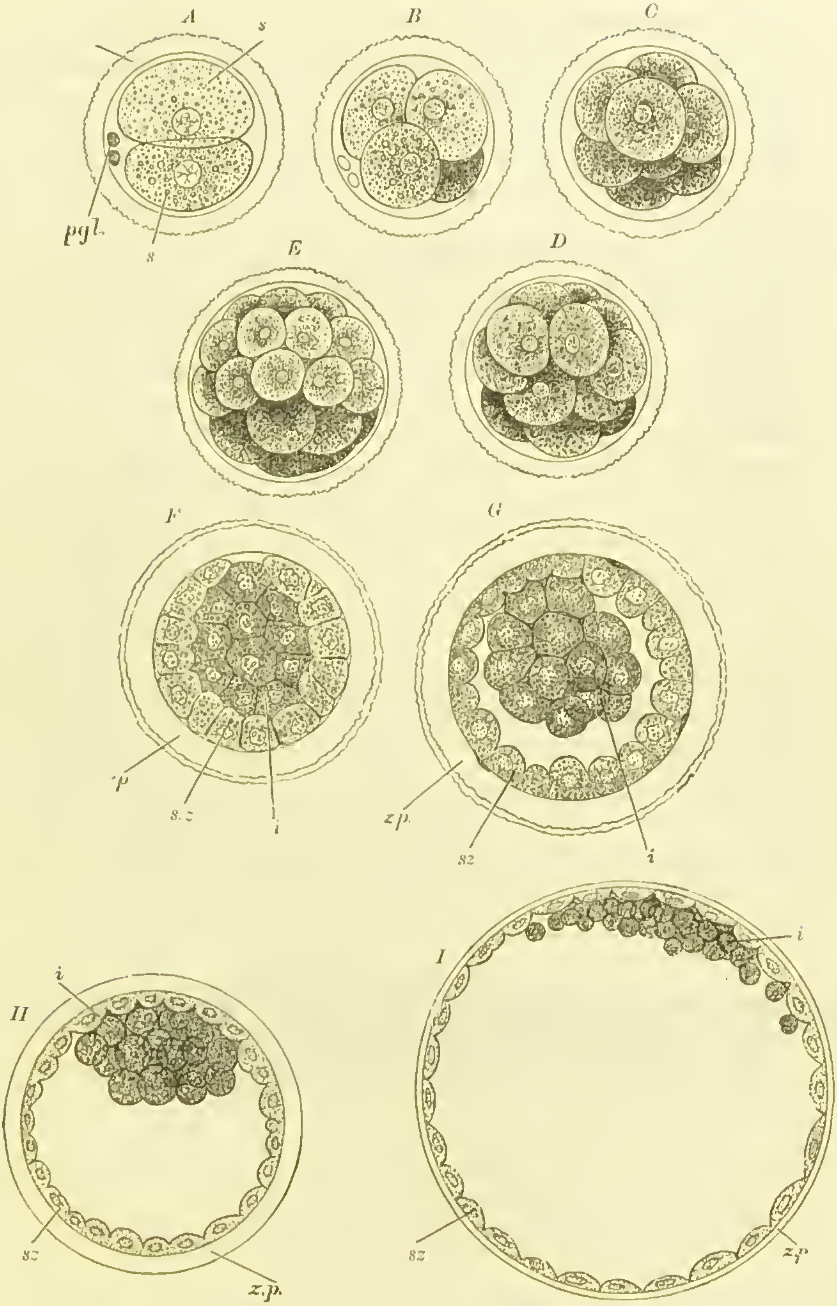


Fig. 33.—Formation of blastoderm in rabbit by division of ovum into a number of cells. (Allen Thomson, after E. v. Beneden.)

A to *E*, division of ovum and formation of "mulberry mass"; *pgl*, polar globules; *s*, *s*, cells of primary division which already show a difference of appearance. This early differentiation is not, however, accepted by most authorities. *F* to *I*, sections of the ovum in subsequent stages. *zp*, membrane of ovum (zona pellucida); *sz*, subzonal layer, by means of which the ovum becomes attached to the uterine mucous membrane; *i*, inner cell-mass, which gives rise to the blastodermic layers. The accumulation of fluid between ectoderm and entoderm in *G*, *H*, and *I* has swollen the ovum out to form the so-called blastodermic vesicle. The subzonal layer of clear cells should be shown in *F* extending all round the inner cell-mass.

of which has also undergone, in the final cell-division by which it was produced, the process of reduction in the number of chromosomes to one half of the normal number. The two reduced nuclei—which are formed respectively from the remainder of the nucleus of the oocyte (ovum) after extrusion of the polar bodies, and from the head of the spermatozoon, which contains the nucleus of the sperm-cell—are known (within the ovum) as the *sperm* and *germ nuclei* or the *male* and *female pro-nuclei.* When these blend, the ovum again contains a nucleus with the number of chromosomes normal to the species. When it divides after fertilisation each daughter cell is found to contain the normal or somatic number of chromosomes, derived from the splitting of both male and female elements, half the number from the one and half from the other.

Formation of the tissues.—It appears to be established beyond doubt that new cells can only be formed from pre-existing cells. In the early embryo the whole body is an agglomeration of cells. These have all been formed from the *ovum* or *egg-cell* (fig. 32), which, after fertilisation, divides first into two cells, these again into two, and so on until a large number of cells (embryonic cells) are produced. These form at first an outer clear stratum lying at the surface (fig. 33, *sz*) and a darker granular mass (*i*) attached to this layer at one part, but elsewhere separated from it by clear fluid. Eventually the cells of the inner mass arrange themselves in the form of a membrane (*blastoderm*) which is composed of three layers. These layers are known respectively as the *ectoderm*, *mesoderm*, and *entoderm*. The ectoderm gives rise to most of the epithelial tissues, and to the tissues of the nervous system;

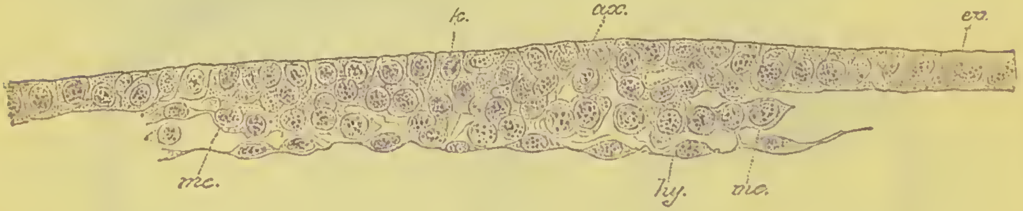


FIG. 34.—SECTION OF BLASTODERM SHOWING THE COMMENCING FORMATION OF THE MESODERM. (Kölliker.)

ep, ectoderm; *hy*, entoderm; *me*, mesoderm; *ax*, axial part of ectoderm with cells undergoing division (*k*). The mesoderm is growing from this part.

the entoderm to the epithelium of the alimentary canal (except the mouth), and the glands in connection with it; and the mesoderm to the connective and muscular tissues.

The tissues are formed either by changes which occur in the intercellular substance, or by changes in the cells themselves; frequently by both these processes combined. Amongst the cells which are least altered from their embryonic condition are the white corpuscles of the blood; these may be regarded, therefore, as typical animal cells.

The histogenetical relation between the three layers of the blastoderm and the several tissues and organs of the body is exhibited in the following table:—

Ectoderm.	The epithelium of the skin or epidermis, and its appendages, viz., the hair, nails, sebaceous and sweat glands, and mammary glands.
	The epithelium of the mouth, and the epithelium of the anus and anal canal.
	The salivary and other glands which open into the mouth. The enamel of the teeth. The gustatory organs.
	The epithelium of the lower part of the urethra and vagina.
	The epithelium of the nasal passages, and of the cavities and glands which open into them.
	The epithelium covering the front of the eye. The epithelium of the lacrymal canals and lacrymal glands. The crystalline lens. The retina. The pars ciliaris retinæ and the pars iridica retinæ. The sphincter and dilatator pupillæ muscles.
	The epithelium lining the membranous labyrinth of the ear. The epithelium lining the external auditory meatus.
	The epithelium lining the central canal of the spinal cord, the aqueduct of Sylvius, and the fourth, third, and lateral ventricles of the brain.
	The tissues of the nervous system.
	The pituitary body. The pineal gland. The medulla of the suprarenal capsules.
Mesoderm.	The connective tissues.
	The blood- and lymph-corpuscles.
	The spleen and other vascular and lymphatic glands.
	The cortex of the suprarenal capsules.
	The epithelial lining of the heart, blood-vessels, lymphatics, and serous membranes (endothelium).
	The epithelium of the uriniferous tubules, and that of the ureters and renal pelves.
	The epithelium of the internal generative organs, including that of the testis and its ducts, and that of the prostatic vesicle, and the generative products in both sexes.
	The epithelium of the ovary, Fallopian tubes, and uterus, and the upper part of the vagina.
	The muscular tissues, voluntary, involuntary, and cardiac (except the plain muscles of the iris and of the sweat glands).[1]
Entoderm.	The epithelium of the alimentary canal (from the pharynx to the lower end of the rectum) and of all the glands which open into it (including the liver and pancreas).
	The epithelium of the Eustachian tube and cavity of the tympanum.
	The epithelium of the larynx, trachea, and bronchi, and of all their ramifications.
	The epithelium of the pulmonary alveoli.
	The thyroid body and parathyroids. The reticulum and the concentric corpuscles of the thymus gland.
	The epithelium of the urinary bladder, of the female urethra, and of the lower part of the vagina.
	The epithelium of the proximal part of the male urethra and its glands.

[1] All the connective tissues, the endothelium (mesothelium) of the vascular system, and the vascular and lymphatic glands are formed from a special part of the mesoderm termed *mesenchyme*, which consists of a syncytium of branched cells with a homogeneous intercellular matrix. Plain muscular tissue is for the most part also formed from mesenchyme, but in certain situations, as in the sweat glands and muscular tissue of the iris, it is said to be ectodermal in origin.

LESSON I.

USE OF THE MICROSCOPE. EXAMINATION OF CERTAIN COMMON OBJECTS.

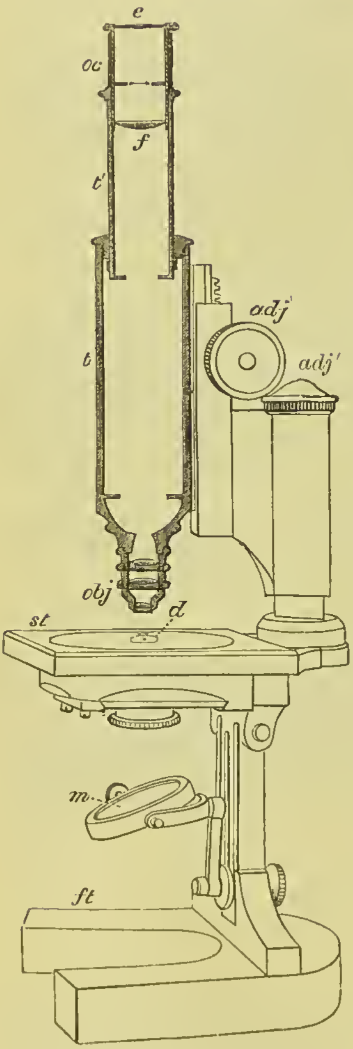


FIG. 35.—DIAGRAM OF MICROSCOPE.

THE requisites for practical histology are a good compound microscope; slips of glass technically known as 'slides,' upon which the preparations are made; pieces of thin glass used as covers for the preparations; a few instruments, such as a microtome, a scalpel, scissors, forceps, and needles mounted in wooden handles; and a set of fluid re-agents for mounting and staining microscopic preparations.[1] A sketch-book and pencil are also necessary, and must be constantly employed.

The microscope (fig. 35) consists of a tube (*t t'*) 160 millimeters (6·4 inches) long having two systems of lenses, one at the upper end termed the 'eye-piece' or 'ocular' (*oc*), the other at the lower end termed the 'objective' (*obj*). For ordinary work there should be at least two objectives—a low power working at about 8 millimeters ($\frac{1}{3}$ inch) from the object, and a high power, having a focal distance of about 3 millimeters ($\frac{1}{8}$ inch); it is useful also to have a lower power (commanding a larger field of view) for finding objects readily, and two or more oculars of different magnification. The focus is obtained by cautiously bringing the tube and lenses down towards the object by the coarse adjustment, which is usually a rack-and-pinion movement (*adj*), and focussing exactly by the fine adjustment, which is always a finely cut screw (*adj'*).

The stage (*st*) upon which the preparations are placed for examination, the mirror (*m*) which serves to reflect light up through the central aperture in the stage and along the tube of the instrument, and the diaphragm (*d*) below the stage which is used to regulate the amount of light thus thrown up, are all parts the employment of which is readily understood. A substage condenser (not shown in the diagram), which serves to concentrate the light thrown up by the mirror to the centre of the object, is valuable when high powers and stained preparations are employed.

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[1] The directions for making the principal fluids used in histological work will be found in the Appendix.

The combinations of objectives and oculars above referred to will generally give a magnifying power of from 50 to 400 diameters, and this is sufficient for most purposes of histology. But to bring out minute points of detail in the structure of cells and of certain tissues examination with much higher magnifying powers may be necessary. Objectives of high power are usually made in immersion-lenses; *i.e.* they are constructed to form a proper image of the object when the lowermost lens of the system is immersed in a layer of liquid which lies on the cover-glass of the object and has a refractive index not far removed from that of the glass itself. For this purpose either water or an essential oil (oil of cedar-wood) is used. The advantages obtained by the employment of these lenses, especially those for oil-immersion, are:—increased working distance from the object, increased angle of aperture with sharper definition of the object, and increased amount of light traversing the microscope.

The best lenses for histological work are made of the so-called "apochromatic' glass; specially constructed 'compensating' eye-pieces and used with these.

A scale for measuring objects should be constructed for each microscope. To do this, put a stage-micrometer (which is a glass slide ruled in the centre with lines $\frac{1}{10}$ and $\frac{1}{100}$ millimeter apart) under the microscope in such a manner that the lines run from left to right (the microscope must not be inclined). Focus them exactly. Put a piece of white card on the table at the right of the microscope. Look through the instrument with the left eye, keeping the right eye open. The lines of the micrometer will appear projected upon the paper. Mark their apparent distance with pencil upon the card, and afterwards make a scale of lines in ink, of the same interval apart. A magnified representation is thus obtained of the micrometer scale. Mark upon it the number of the eye-piece and of the objective, and the length of the microscope-tube. This scale-card will serve for the measurement of any object without the further use of the micrometer. To measure an object, place the scale-card upon the table to the right of the microscope and view the object with the left eye, keeping the right eye open. The object appears projected upon the scale, and its size in $\frac{1}{10}$ or $\frac{1}{100}$ of a millimeter can be read off. It is essential that the same objective and eye-piece should be employed as were used in making the scale, and that the microscope tube should be of the same length. The lines on English stage-micrometers are usually ruled $\frac{1}{100}$ and $\frac{1}{1000}$ inch apart.[1]

Before beginning the study of histology the student should endeavour to familiarise himself with the use of the microscope, and at the same time learn to recognise some of the chief objects which are liable to occur accidentally in microscopic specimens. On this account it has been considered desirable to introduce directions for the examination and recognition of starch-granules, moulds and torulæ, air-bubbles, linen, cotton, and woollen fibres, and the usual constituents of the dust of a room, into the first practical lesson (fig. 36).

1. Examination of starch-granules. Gently scrape the cut surface of a potato with the point of a knife; shake the starch-granules so obtained into a drop of water upon a clean slide and apply a cover-glass.

With the low power the starch granules look like dark spects differing

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[1] For the method of measuring with an ocular micrometer, and for determining the magnifying power of a microscope, the reader is referred to the author's *Course of Practical Histology.*

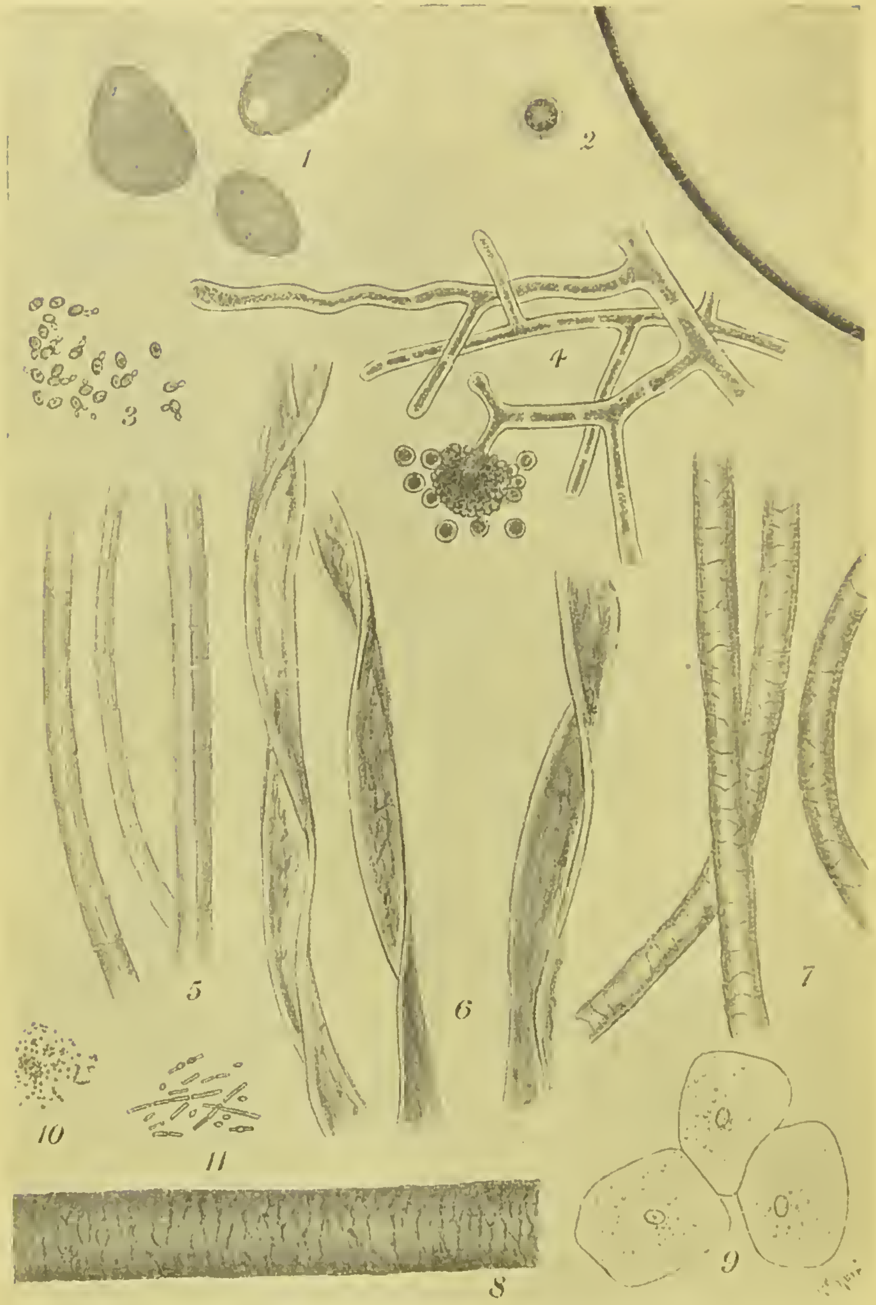

FIG. 36.—OBJECTS WHICH MAY BE ACCIDENTALLY PRESENT IN MICROSCOPIC PREPARATIONS.

1, Starch granules; 2, a small air bubble and part of a large one; 3, yeast torulæ; 4, a mould (Aspergillus glaucus); 5, linen fibres; 6, cotton fibres; 7, wool; 8, hair, human; 9, epithelium scales; 10, micrococci; 11, bacilli and spores (B. subtilis). Magnified about 250 diameters.

considerably in size; under the high power they are clear, flat, ovoid particles (fig. 36, 1), with a sharp outline when exactly focussed. Notice the change in appearance of the outline as the microscope is focussed up and down. On close examination fine concentric lines are to be seen in the granules, arranged around a minute spot which is generally placed eccentrically near the smaller end of the granule. Sketch two or three starch granules.

Notice the appearance of air-bubbles in the water (fig. 36, 2). If comparatively large they are clear in the middle, with a broad dark border due to refraction of the light; if small they may look entirely dark.

Pass a drop of dilute iodine solution under the cover-glass, and observe the staining of the starch granules.

2. Examine some yeast which has been grown in solution of sugar. Observe the yeast-particles or torulæ, some of them budding (fig. 36, 3). Each torula contains a clear vacuole, and has a well-defined outline, due to a membrane. Sketch two or three torulæ.

3. Examine some mould in water. Notice the long branching filaments (hyphæ), and also the torula-like particles (spores) from which hyphæ may in some instances be seen sprouting (fig. 36, 4). Sketch part of a hypha.

4. Examine fibres of linen and of cotton in water, using a high power. Compare the well-defined, rounded, relatively straight or but slightly twisted linen, with the longer, broader but thinner, and more twisted cotton fibres (fig. 36, 5, 6). Sketch one of each kind.

5. Mount one or two hairs from the head in water and look at them first with the low, then with the high power (fig. 36, 8). Examine also fibres from any woollen material and compare them with the hairs. They have the same structure, although the wool is finer and is curled (fig. 36, 7); its structure may be obscured by the dye. Draw one or two of each.

6. Examine a drop of hay infusion, which has been standing a day or two, for bacteria and other putrefactive organisms (fig. 36, 10, 11). The active movements which these exhibit are due to minute cilia or flagella, which can only be made visible by special staining methods and a very high magnifying power. Notice that minute particles, organic or inorganic, which occur in this or other fluids may be seen to exhibit a peculiar tremulous dancing movement which is known as the Brownian' movement.

7. Examine some dust of the room in water with a high power. In addition to groups of black particles of carbon (soot) there will probably be seen fibres of linen, cotton, or wool, and shed epithelium-cells (fig. 36, 9) derived from the epidermis.

8. Examine a drop of milk with the high power. Notice the particles of cream. Their fatty nature is shown by their high refracting power, and by their staining reactions with dyes which have a special affinity for fats, such as osmic acid or Soudan III.

LESSONS II. AND III.

STUDY OF THE HUMAN BLOOD-CORPUSCLES.

1. Having cleaned a slide and cover-glass, prick the finger above the nail or on the pulp, and mount the small drop of blood which issues from the prick as quickly as possible, so that it has time neither to dry nor to coagulate. Examine it at once with the high power.

Note (*a*) the coloured corpuscles mostly in rouleaux and clumps, but some lying apart seen flat or in profile; (*b*) the colourless corpuscles, easily made out if the cover-glass is touched by a needle, on account of their tendency to stick to the glass, whilst the coloured corpuscles are driven past by the currents set up; (*c*) in the clear spaces, fibrin-filaments and elementary particles or blood-platelets.

Sketch a roll of coloured corpuscles and one or two colourless corpuscles. Count the number of colourless corpuscles in a field of the microscope.

2. To be made as in § 1, but the drop of blood is to be mixed upon the slide with an equal amount of isotonic salt solution[1] so that the red corpuscles tend to be less massed together, and their peculiar shape is better displayed.

Sketch a red corpuscle seen on the flat and another in profile (or optical section). Also a crenated corpuscle.

Measure ten red corpuscles, and from the results ascertain the average diameter of a corpuscle. Measure also the largest and the smallest you can find.

3. Make a preparation of blood as in § 1 and put it aside to coagulate. Keep the edges from drying by placing it in a moist chamber or by occasionally breathing upon it. After a few minutes place a drop of 1 p.c. methyl violet at one edge of the cover and allow this to pass in and mix with the blood: it may be drawn through the preparation by applying a very small fragment of blotting paper to the opposite edge. The dye stains the nuclei of the white corpuscles, the blood-platelets, the network of fibrin-filaments, and the membranes of the red blood-corpuscles.

The three preparations just described cannot be kept, but the two following will serve as permanent preparations of blood:—

4. To fix and stain the coloured corpuscles:—Place upon a slide a drop of 1 p.c. osmic acid mixed with an equal amount of saturated aqueous solution of eosin. Prick the finger, and mix the blood directly with the coloured fluid, stirring them together with a needle. Cover the mixture and put aside for an hour, protected from evaporation; then place a very small drop of glycerine and water at the edge of the cover-glass. When this has passed under, *i.e.* in about half an hour or more, fix the cover-glass with gold size.

5. To study the granules of the colourless corpuscles and their different reactions to staining reagents, a film of blood is inclosed between two cover-

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[1] A solution of sodium chloride containing from 7·5 to 9 grammes to the litre. Ringer's solution may also be used. This is made by saturating normal or isotonic salt solution with calcium phosphate, and adding ten milligrammes of potassium chloride to each litre.

glasses, which are at once separated and the film on each quickly dried in the air. A slide may be used instead of a cover-glass; the drop of blood is placed close to the ground edge of one slide and this is drawn evenly over the middle of another. The films are fixed by immersion for one hour or more in a mixture of alcohol and ether, equal parts of each. A more rapid but less sure method of fixation is to pass the slide two or three times rapidly over the flame of a spirit lamp. The film is then stained by (1) a saturated solution of eosin in 75 p.c. alcohol (three minutes), after which it is rinsed with water, and treated with (2) a 1 p.c. solution of methylene blue (one

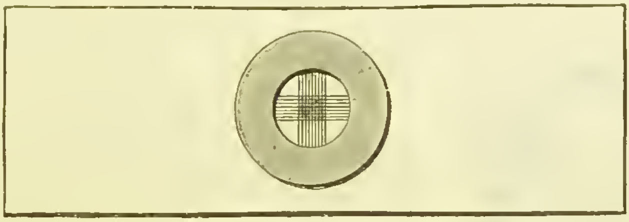

FIG. 37A.—HÆMACYTOMETER SLIDE, RULED IN SQUARES FOR THE ENUMERATION OF BLOOD-CORPUSCLES.

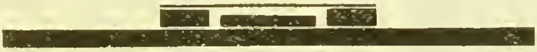

FIG. 37B.—DIAGRAM OF A SECTION THROUGH THE HÆMACYTOMETER SLIDE.

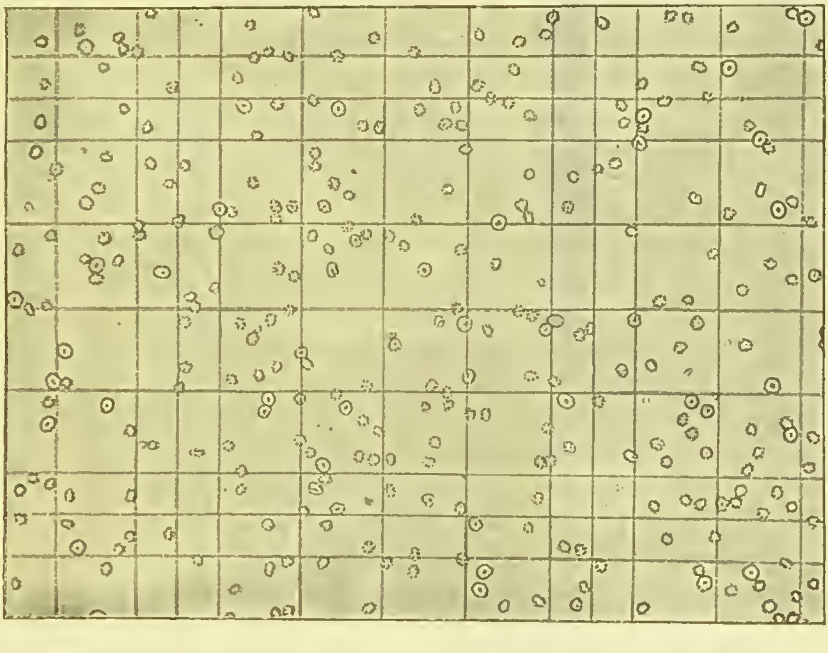

FIG. 38.—APPEARANCE OF THE SQUARES OF THE THOMA-ZEISS HÆMACYTOMETER WHEN USED FOR A BLOOD-COUNT. Magnified 200 diameters.

minute). The film is again rinsed with water, rapidly dried, and mounted in xylol balsam or dammar.[1]

6. Mount in xylol balsam or dammar sections of marrow from a long bone (rabbit) fixed with mercuric chloride or formol and stained with eosin and methylene blue. Observe the fat-cells, the supporting reticular tissue, the proper marrow-cells in this tissue, the myeloplaxes and the erythroblasts.

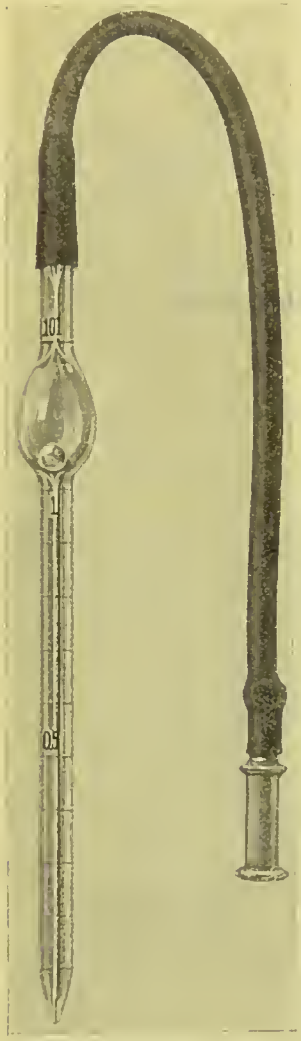

Fig. 39.—Pipette used for the Thoma-Zeiss hæmacytometer.

7. Tease in salt solution or serum some of the red marrow from the rib of a recently killed animal. Observe and sketch the proper marrow cells (myelocytes) and look for myeloplaxes (giant-cells) and nucleated coloured blood-corpuscles (erythroblasts.)

8. Make a film preparation of red marrow by smearing a little upon a cover-glass or slide, allowing it to dry quickly, and placing it in a mixture of equal parts of ether and alcohol. After an hour or more in this, the preparation may be stained with eosin and methylene blue in exactly the same way as a film preparation of blood (see § 5), and mounted in xylol balsam or dammar.

9. Enumeration of the blood-corpuscles. This is done by some form of blood counter such as the hæmacytometer of Gowers, or the similar apparatus of Thoma. This instrument consists of a glass slide (fig. 37), the centre of which is occupied by a small glass plate having its upper surface ruled into $\frac{1}{10}$ millimeter squares, subdivided into smaller portions to facilitate enumeration, and surrounded by a glass ring $\frac{1}{10}$ mm. thicker than the ruled glass plate (in Gower's instrument, the ruling is in $\frac{1}{5}$ mm. squares with a ring $\frac{1}{5}$ mm. thick). There must also be provided a pipette for measuring the blood, and a mixing vessel which in Thoma's instrument is combined with the pipette (fig. 39). The diluting solution may either be that of Hayem, viz., distilled water 200 c.c., sulphate of soda 5 grms., common salt 1 grm., corrosive sublimate 0·5 grm., or that of Morcano, viz., 97 cc. of a solution of sulphate of soda (in distilled water) of sp. gr. 1020, to which is added chloride of sodium 1 grm., and formol 3 cc. The finger is pricked, and the pipette filled exactly with blood up the 1 mark.[2] The pipette is then filled with diluting solution up to the 101 mark, the blood being thereby drawn up into the mixing vessel,

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[1] Other stains, such as Leishman's, Ehrlich's tri-acid, and the Ehrlich-Biondi, may also be employed for films. These require only one operation.

[2] In Gower's apparatus one pipette is used for measuring the blood and another for the diluting fluid, and the two are mixed in a small glass vessel with the aid of a glass rod; these are easier to clean than the combined measuring and mixing pipette of the Thoma apparatus.

where it is thoroughly mixed with the solution by shaking the included glass ball (fig. 39). It is thus diluted 100 times. After expelling the clean fluid in the capillary part, a drop of the mixture is placed in the centre of the cell, and the cover-glass is gently laid on so as to touch the drop, which thus forms a layer $\frac{1}{10}$ mm. thick between the ruled glass plate and cover-glass. In a few minutes the corpuscles have sunk to the bottom of the layer of fluid and rest on the squares (fig. 38). The number in ten of the $\frac{1}{10}$ mm. squares is then counted, and this, multiplied by 100, gives the number in a cubic millimeter of the mixture, or if again multiplied by 100 (the amount of dilution) the number in a cubic millimeter of blood.

For the enumeration of the white corpuscles the blood is diluted only 10 times instead of 100 times. It is also convenient to use one half per cent. solution of acetic acid just coloured with methyl violet as a diluent (Thoma). This destroys the coloured corpuscles and stains the nuclei of the white.

The coloured blood-corpuscles.—The coloured corpuscles are composed of a delicate colourless highly elastic (? protoplasmic) *envelope*, and *coloured fluid contents*, consisting mainly of a solution of hæmoglobin. The existence of such an envelope is shown by the osmotic effect of water upon the corpuscle, which passing in through the envelope, distends it, and eventually sets free the contents. The description which is current in many text-books that the red corpuscles consist of a porous solid *stroma*, permeated with dissolved hæmoglobin, is incompatible with this and similar reactions. Moreover, the envelope can be distinctly seen with the microscope, especially in the amphibian corpuscle, and can be stained by reagents. The envelope contains lipoid substances in considerable amount, and these substances impart a certain greasiness to the surface of the corpuscle. It is in all probability due to such greasiness that the corpuscles run together into rouleaux when the blood comes to rest (see p. 50).

Under the microscope blood is seen to consist of a clear fluid (*plasma*), in which are suspended the *blood corpuscles* (fig. 40). The latter are of two kinds: the *red* or *coloured* (*erythrocytes*), which are by far the most numerous, and the *white*, *pale*, or *colourless* (*leucocytes*). In addition to these more obvious corpuscles, blood contains a variable number of minute particles which were termed by Zimmermann the *elementary particles of the blood*, but which are now more usually known as the *blood-platelets* on account of their flattened form.

Erythrocytes.—When seen singly the coloured corpuscles are not distinctly red, but appear of a reddish-yellow tinge. In the blood of man and of all other mammals, except the Camelidæ, they are biconcave circular disks. Their central part usually has a lightly shaded aspect under a moderately high power, but this is due to their biconcave shape, not to the presence of a nucleus. They have, as just stated, a strong tendency to become aggregated into rouleaux and clumps when the blood is at rest, but if it is disturbed they readily become separated.

If the density of the plasma is increased in any way, as by evaporation, many of the red corpuscles become shrunken and crenated by the passage of water out of the corpuscle. On the other hand, a diminution in the density of the plasma tends to cause the red corpuscles to become cup-shaped, but it is erroneous to describe this as the normal form of the corpuscle, although there are a certain number of cup-shaped corpuscles to be seen in the circulating blood when this is examined in transparent parts of animals. By far the largest number, however, are biconcave.

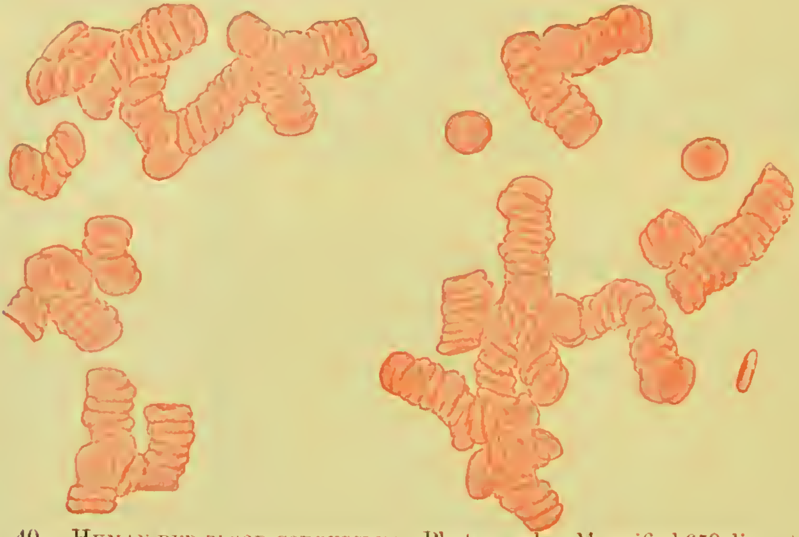

Fig. 40.—Human red blood-corpuscles: Photograph. Magnified 650 diameters.

The average diameter of the human red corpuscle is 0·0075 millimeter[1] (about $\frac{1}{3200}$ inch), but a few will always be found somewhat larger (0·0085) and a few somewhat smaller (0·0065 mm.).[2]

There are from four to five millions of coloured corpuscles in a cubic millimeter of blood.

Leucocytes.—The colourless corpuscles of human blood are protoplasmic cells, averaging 0·01 mm. ($\frac{1}{2500}$ inch) in diameter when spheroidal, but they vary much in size and shape. They are far fewer than the coloured corpuscles, usually numbering not more than eight to ten thousand in a cubic millimeter (about 1 to 600 red corpuscles). Moreover, they are specifically lighter, and tend to come to the surface of the preparation. If examined immediately the blood is drawn, they are spherical in shape, but soon become flattened and then irregular in form (fig. 3), and their outline continually alters, owing to the amœba-like changes to which they are subject. In some kinds (*phagocytes*) the protoplasm tends to take in foreign particles with which the cells come in contact; in others there seems to be little or no such tendency. Some of the colourless corpuscles are very pale and filled with fine granules, others contain coarser and more distinct granules in their protoplasm; others again have a hyaline protoplasm without any apparent granules. In some corpuscles (*lymphocytes*) the protoplasm forms only a relatively small proportion as compared with the nucleus.

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[1] Also expressed as 7·5 μ or microns; a micron being $\frac{1}{1000}$ millimeter.

[2] The following list gives the diameter in parts of a millimeter of the red blood-corpuscles of some of the common domestic animals:—Dog, 0·0073; rabbit, 0·0069; cat, 0·0065; goat, 0·0041.

Leucocytes are classified according to the character and appearance of the nucleus and the nature and staining qualities of the granules in their protoplasm. Some granules are readily stained by basic dyes such as methylene blue; such granules are accordingly termed *basiphil.* Distinct coarse basiphil granules are, however, rare in normal blood, although cells with these granules are normally present in the marrow and in some connective tissues, and make their appearance in the blood in leucocythæmia. On the other hand, some granules more readily take up colour from acid dyes, such as eosin; these have been termed *oxyphil* or *eosinophil.* Others possess granules (*amphophil*) which are stained by both acid and basic dyes; and others chiefly by neutral dyes (*neutrophil*). In some cells more than one kind of granule is met with. The protoplasm may also contain clear spaces or vacuoles. Each

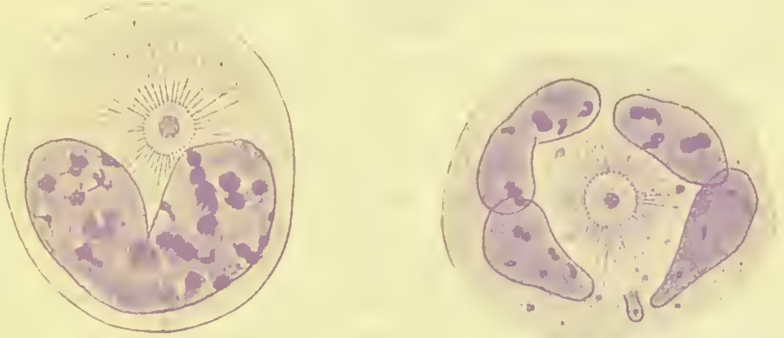

FIG. 41.—TWO LEUCOCYTES OF LEPIDOSIREN, SHOWING ATTRACTION-SPHERE. (T. H. Bryce.)

A, a macrocyte with kidney-shaped nucleus.
B, a polymorph, with lobed nucleus (the threads of chromatin joining the lobes are not shown).

leucocyte has at least one nucleus, which is difficult to see in a fresh preparation, but is easily seen after the action of most reagents and after staining. There is also a centrosome with attraction-sphere (fig. 41, and fig. 11, p. 9), but special methods of staining are necessary to exhibit these.

The following are the chief varieties of leucocytes:—1. *Polymorphs.* Cells with lobed or multipartite nuclei and a relatively large amount of protoplasm, which is highly amœboid. These are often termed multi-(poly-)nuclear, but the nucleus is rarely if ever multiple, its several parts being nearly always joined by threads of nuclear substance. The cells in question vary in size, but when spherical are usually not quite 0·01 mm. in diameter. Their protoplasm stains with eosin, this being due to the presence of fine oxyphil granules (Kanthack and Hardy). They are highly amœboid and phagocytic, and constitute from sixty to seventy per cent. of all the leucocytes of the blood (fig. 42, *a*; see also fig. 67).

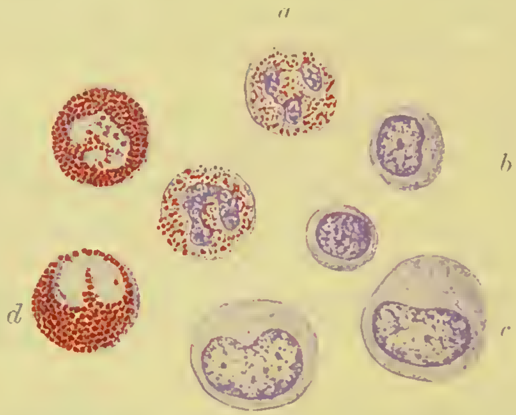

FIG. 42.—VARIOUS KINDS OF COLOURLESS CORPUSCLES, SHOWING THE DIFFERENT CHARACTERS OF THE GRANULES. (From a film preparation of normal human blood.) Two of each kind have been drawn.

2. *Lymphocytes.*—These are small cells, with a limited amount of clear protoplasm around the nucleus, which is simple, not lobed or divided (fig, 42, *b*; see also fig. 15). The amœboid phenomena are less marked in them than in the other varieties of leucocytes. The protoplasm stains with methylene blue. They are about 0·0065 mm. in diameter, but some are larger and appear to be transitional between this and the next variety. They constitute from fifteen to thirty per cent. of the total number of leucocytes in the blood. They are relatively more numerous in infancy.

3. *Macrocytes.*—Large uninucleated cells similar to the last, but larger, and containing much more protoplasm (fig. 42, *c*). Some of

these which are smaller are regarded as transitional forms from the last variety. The nucleus may be spherical, oval, or kidney-shaped. The protoplasm is hyaline; it stains slightly with methylene blue, perhaps owing to very fine basiphil granules. These cells are amœboid and phagocytic. Including the transitional forms, they constitute about five per cent. of all the leucocytes in blood.

4. *Oxyphils.* —These are characterised by their coarse granules, which stain deeply with acid dyes, such as eosin. Their average diameter in the spherical condition is 0·01 mm. The nucleus may be simple or lobed (fig. 42, *d*; see also fig. 69). They are amœboid, but less actively so than the finely granular cells. They are more variable in number than the other varieties, constituting sometimes not more than one per cent., and at other times as much as ten per cent. of the total leucocytes of blood.

5. *Basiphils.*—These are rarely if ever found in normal blood (adult), but occur in children, and in certain pathological conditions affecting the bone marrow.

Blood-platelets.—In the clear fluid in which the blood-corpuscles are suspended, a network of fine straight intercrossing filaments (fibrin) soon makes its appearance (fig. 43). These often seem to radiate from minute round colourless discoid particles less than one-third the diameter of a red corpuscle, either separate or collected into groups or masses, of variable, sometimes of considerable, size. These are the *elementary particles*, *blood-platelets*, or *thrombocytes*. In the blood-vessels they are discrete, but immediately clump together in drawn blood (fig. 45). If, however, the blood is examined on agar jelly containing certain salts in definite proportions, the platelets can be kept separate, and may then be submitted to very high powers of the microscope. The result of such examination seems to show that the blood-platelets are not mere inert particles, as has generally been supposed, but that they are protoplasmic and amœboid, and that each one contains a nucleus (fig. 46); that they are in fact minute cells (Deetjen). Blood-platelets vary greatly in number: they are estimated by Brodie and Russell to amount to from 5 millions to 45 millions in the cubic centimeter of blood.

After blood is drawn, and when it comes in contact with foreign matter or injured tissue, the blood-platelets undergo a remarkable change, giving off viscid threads which adhere together, and also fix themselves to adjacent structures. This will be again referred to when amphibian blood is dealt with.

Fatty particles, derived from the chyle, may also occur in the plasma.

Development of red blood-corpuscles.—In the mesoderm of the embryo, at first in that of the yolk sac and subsequently in the body of the embryo, the blood-corpuscles make their appearance as amœboid nucleated cells, apparently derived by mitotic division from some of the ordinary mesoderm cells (fig. 47). These are the *blood-cells* or *primitive hæmatoblasts.* They resemble lymphocytes, but after a time the protoplasm of some of them is found to contain hæmoglobin (fig. 48); they may now be termed *primitive erythroblasts.* Soon after their appearance they are found to be enclosed within a syncytium of the mesoderm or mesenchyme (fig. 49), which forms a network, at first incomplete but afterwards complete, at the nodes of which are enlargements containing groups of the primitive erythroblasts. This gives to the tissue the appearance of isolated reddish spots—the blood islands of Pander. The network becomes hollowed out by an accumulation of fluid in the syncytial protoplasm, and thus are

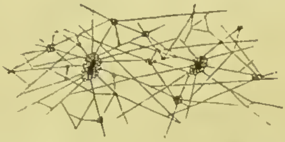

Fig. 43.—Network of fibrin, shown after washing away the corpuscles from a preparation of blood that has been allowed to clot; many of the filaments radiate from small clumps of blood-platelets.

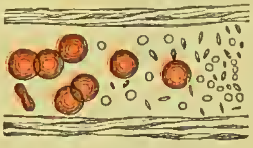

Fig. 44.—Blood-corpuscles and elementary particles or blood-platelets, within a small vein. (From Osler.)

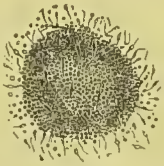

Fig. 45.—A mass of blood-platelets, from human blood. (Osler.)

A few at the edge are detached from the rest. The preparation had been kept in salt solution on the warm stage for some time, thus causing a partial breaking up of the mass of platelets. These will be observed to have filaments attached to them.

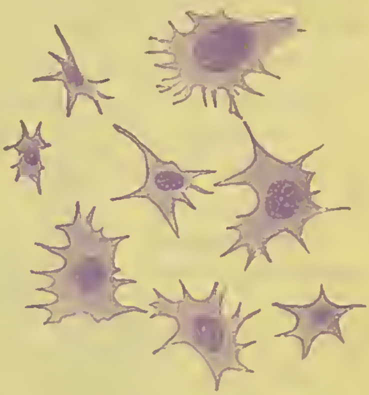

Fig. 46.—Blood-platelets, highly magnified, showing the amœboid forms which they assume when examined under suitable conditions, and also exhibiting the chromatic particle which each platelet contains, and which has been regarded as a nucleus. (After Kopsch.)

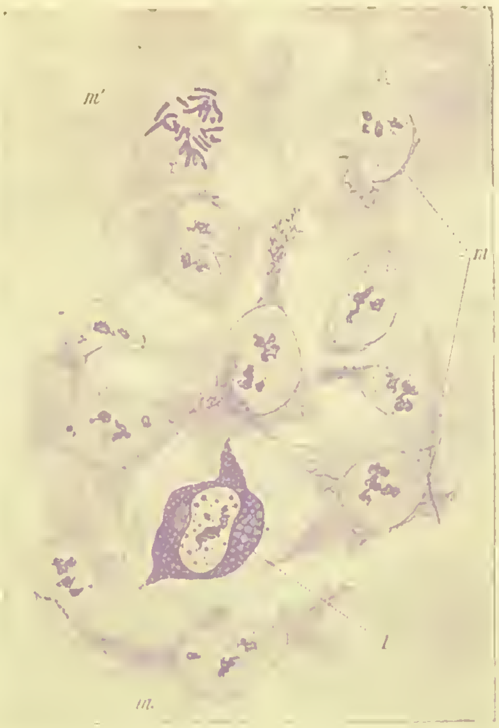

Fig. 47.—Mesoderm cells of rabbit embryo, united to form a syncytium. (Maximow.)

m, ordinary mesoderm cells; *m'*, a cell in karyokinesis; *l*, a primitive blood-cell.

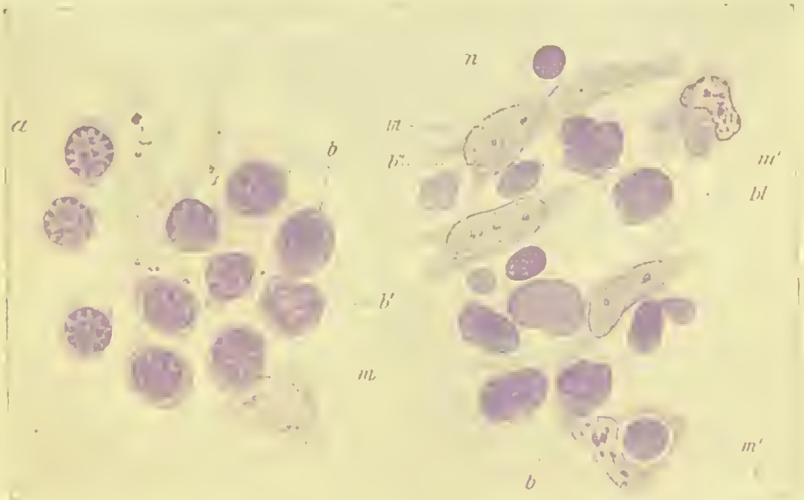

Fig. 48.—Groups of primitive erythroblasts in mesoderm of embryo rabbit. (Maximow.)

a, normoblasts; *b*, *b'*, erythroblasts; *m*, mesoderm cells; *m'*, mesoderm cells containing hæmoglobin; *b''*, extrusion of nucleus from an erythroblast; *n*, an extruded nucleus; *bl*, an erythrocyte.

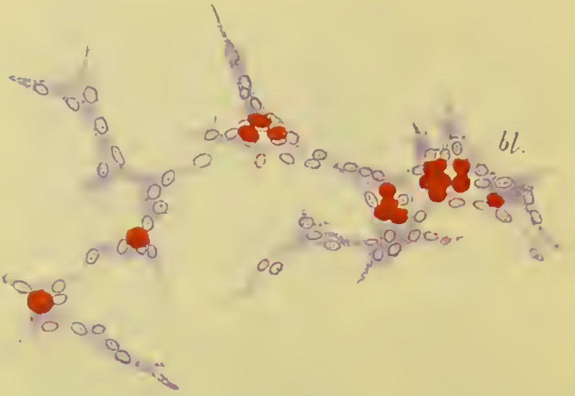

FIG. 49.—DEVELOPMENT OF BLOOD-VESSELS AND BLOOD-CORPUSCLES IN THE VASCULAR AREA OF THE GUINEA-PIG.

bl, blood-corpuscles becoming free in the interior of a nucleated protoplasmic mass.

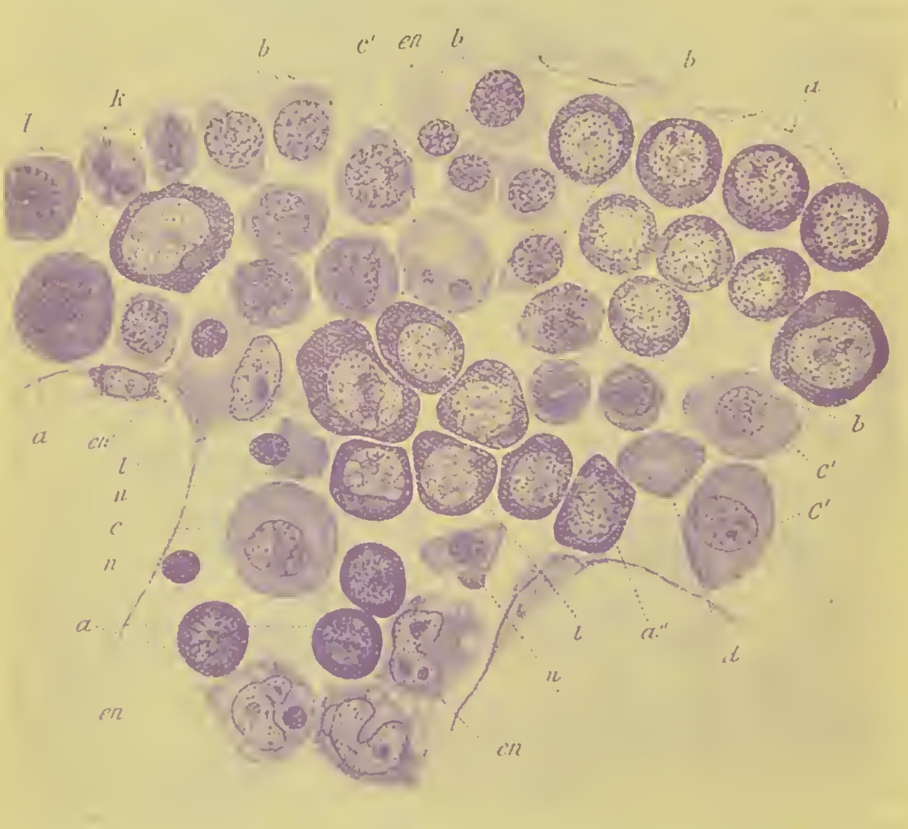

FIG. 50.—PART OF A BLOOD-VESSEL FROM THE YOLK SAC OF THE RABBIT EMBRYO, SHOWING THE CHANGES WHICH OCCUR IN THE PROCESS OF FORMATION OF ERYTHROCYTES. (Maximow.)

a, *a'*, *a''*, megaloblasts; *b*, normoblasts in process of transformation into erythroblasts; *c'*, erythroblasts, the nuclei of which are becoming less chromatic and in one or two cells have almost disappeared; *d*, an erythrocyte fully formed but not discoid; *en*, *en'*, phagocytic endothelial cells; *l*, lymphocytes; *k*, a divided lymphocyte; *n*, erythroblasts somewhat shrunken and with atrophying nucleus; *n*, a nucleus becoming extruded.

produced a number of capillary blood-vessels, within which the coloured nucleated cells are set free as embryonic blood-corpuscles. Within the circulation these multiply by mitotic division, and thus become rapidly more numerous. The primitive erythroblasts are relatively large, and resemble the megaloblasts of bone-marrow (see p. 43), but after division they give rise to smaller erythroblasts, similar to the normoblasts of bone-marrow. These form the nucleated coloured blood-corpuscles (erythroblasts) of the embryo during the first few weeks of intrauterine life. They also multiply by mitotic division, so that the number of nucleated coloured blood-corpuscles becomes considerable, a certain number of colourless cells also appearing

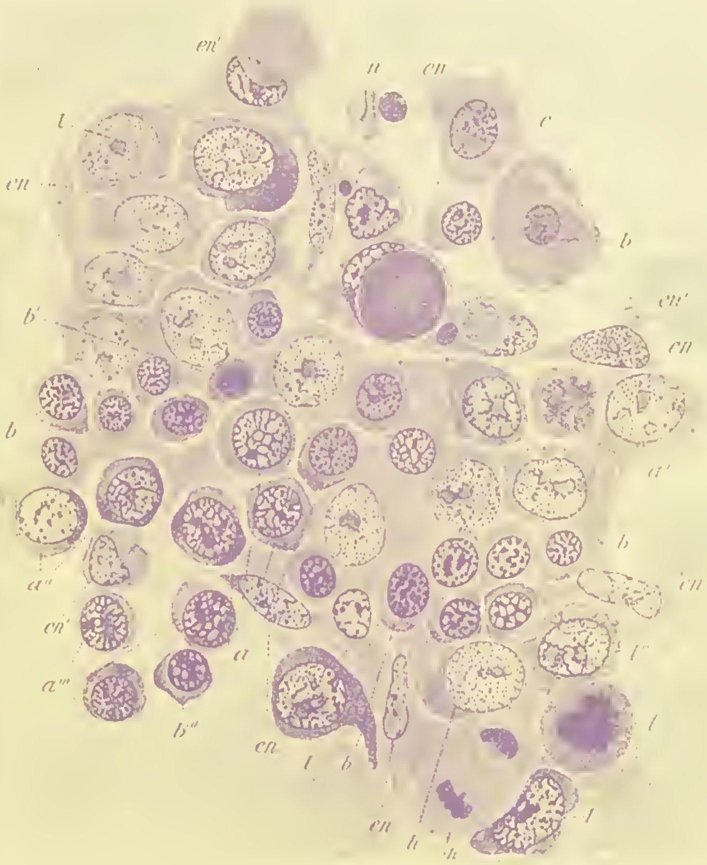

FIG. 51.—FORMATION OF ERYTHROBLASTS IN LIVER OF EMBRYO RABBIT. (Maximow.)

en, en′, endothelial cells of vessels; a, a′, a″, a‴, megaloblasts; b, b′, b″, b‴, normoblasts; c, erythroblasts; l, l′, l″, lymphoblasts; h, hepatic cells; n, a nucleus becoming extruded from a small erythroblast.

amongst them. After a time, ordinary non-nucleated blood-disks (erythrocytes) of very variable size begin to appear amongst the nucleated cells, and these last become relatively fewer in number. Before the middle of intrauterine life the erythroblasts have nearly disappeared from the blood, and their place is taken, as in the adult, by erythrocytes, the erythroblasts being confined to bone marrow, and the various changes in them which lead to the development of erythrocytes, now taking place in the marrow instead of in the blood-vessels as is the case in the early embryo (fig. 50).

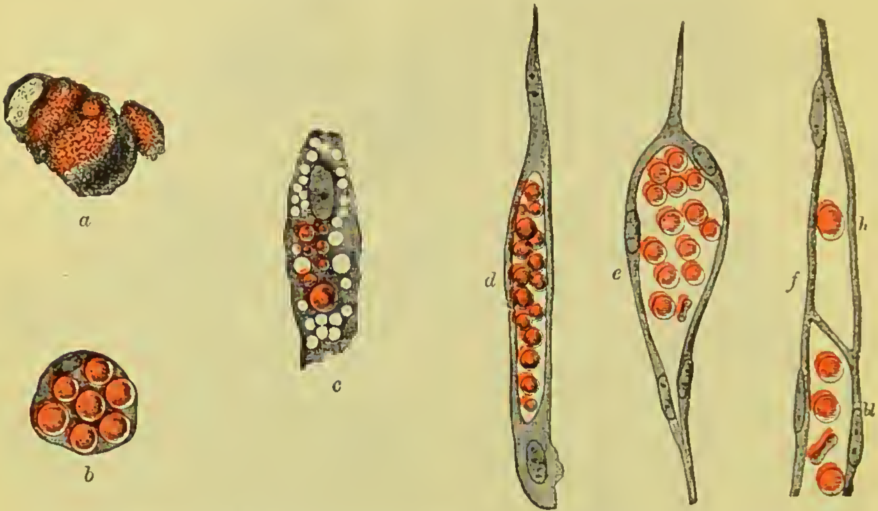

Fig. 52.—Blood-corpuscles developing within connective-tissue cells.

a, a cell containing diffused hæmoglobin; *b*, a cell filled with coloured globules; *c*, a cell containing coloured globules in the protoplasm, within which also are numerous vacuoles; *d*, an elongated cell with a cavity in its protoplasm occupied by fluid and blood-corpuscles mostly globular; *e*, a hollow cell, the nucleus of which has multiplied. The new nuclei are arranged around the wall of the cavity, the corpuscles in which have now become discoid; *f*, shows the mode of union of a 'hæmapoietic' cell, which in this instance contains only one corpuscle, with the prolongation (*bl*) of a previously existing vessel.

The multiplication of erythroblasts by mitosis, and the formation from them of erythrocytes, is found to go on in the blood-vessels of the embryonic liver long after it has ceased to be observed in other vessels (fig. 51). According to Maximow it is not confined to the blood-vessels, but goes on also in the hepatic tissue between the vessels. In birds it continues to occur throughout life within the blood-vessels of the bone-marrow.

Erythrocytes are also formed at a somewhat later stage of development within certain cells of the connective tissue (*vasoformative cells*), a portion of the substance of the cell becoming coloured by hæmoglobin, and separated into globular particles (fig. 52, *a*, *b*, *c*), which are gradually moulded into disk-shaped red corpuscles. In the meantime the cells become hollowed out, and join with similar neighbouring cells to form blood-vessels (fig. 52, *d*, *e*, *f*). The process is therefore somewhat different from that in the early embryo, since cell-nuclei are not included in the hæmoglobin-holding protoplasm from which the erythrocytes are formed.

It has been suggested by some writers that the vasoformative cells containing coloured corpuscles in various stages of formation are in reality portions of an already formed vascular network which is undergoing atrophy; and that the corpuscles within such cells are not in process of formation but of disappearance. But since the appearances in question are seen in parts in which vascular tissues (such as fat) are undergoing not atrophy but formation; and since, moreover, the hæmatoidin crystals and pigment granules which are characteristic of the disintegration of erythrocytes within cells are not present, it seems more reasonable to interpret the appearances as indicative of intracellular development of blood-corpuscles by differentiation of part of the protoplasm of the vasoformative mesenchyme cell, rather than as a degeneration of already formed blood-vessels and blood-corpuscles.

Formation in bone-marrow.—The marrow of bone is of a yellow colour in the shafts of the long bones of most animals, and is there largely composed of adipose tissue, but in the shafts of the long bones of some animals, and in the cancellated tissue of most, it has relatively few fat cells, and is usually red, the colour being partly due to the large amount of blood in its vessels. This red marrow (figs. 53, 54) is chiefly composed of protoplasmic cells—the *myelocytes* or *marrow-cells*—which resemble rather large blood leucocytes, and, like these, are amœboid. They also exhibit the same kind of differences as to the character of the granules which they contain, some being oxyphil and others amphophil or neutrophil. But while the blood-leucocytes rarely contain any coarse basiphil granules, some of the marrow-cells contain these in considerable numbers. There are also to be seen mingled with the marrow-leucocytes a number of corpuscles somewhat smaller in size, nucleated, and at least some of them amœboid, but of a reddish tint (fig. 54, *e′*). These cells, which by mitotic division produce *erythroblasts*, resemble the nucleated coloured corpuscles of the embryo.

They vary in size, most measuring about ·007 mm. (normoblasts), but some being considerably larger (megaloblasts), and others considerably smaller (microblasts). The red disks are formed from the erythroblasts by the nucleus disappearing and the coloured protoplasm becoming moulded into a discoid shape. At what time this formation of blood-corpuscles in the bone-marrow begins has not been ascertained, but after it has commenced it continues throughout the whole of life—the red marrow, especially that of the ribs, being especially active in this respect. In mammals the multiplication

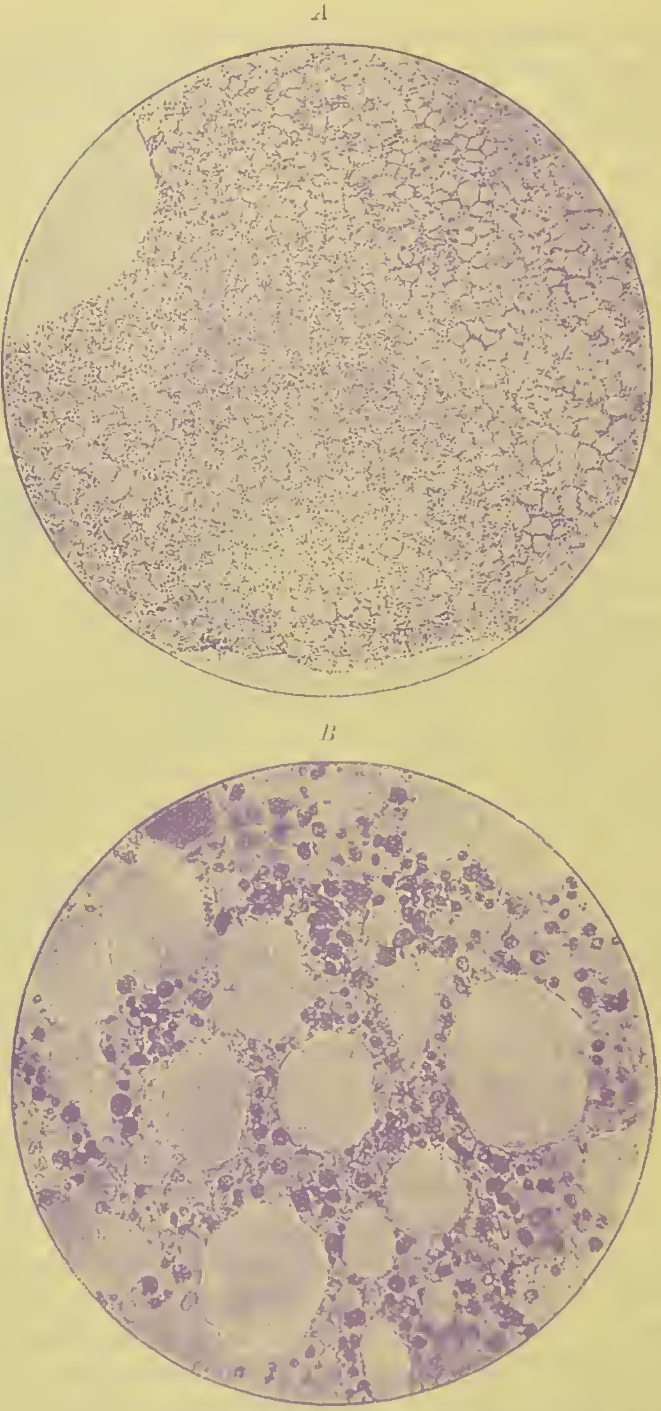

Fig. 53.—Sections of red marrow. (Carnegie Dickson.)

A, Magnified 45 diameters. *B*, Magnified 300 diameters.
The clear spaces are due to the presence of fat-cells.

of nucleated coloured corpuscles appears to take place within the tissue of the marrow external to the blood-vessels. It is uncertain to what extent the capillary vessels of the marrow are limited by a complete endothelium (see next page), but in any case the formed erythroblasts seem to readily pass into the blood stream. In birds the formation of erythroblasts is confined to the large blood-channels of the marrow, and the transformation into erythrocytes occurs within these channels.

Many of the erythroblasts are in process of mitotic division. Others are seen with the nucleus in a more or less atrophied condition; from this it may be inferred that the transformation into a discoid blood-corpuscle is accompanied by the disappearance of the nucleus. Whether it eventually becomes extruded or simply undergoes complete atrophy is uncertain. The marrow also contains a number of very large cells, the *giant-cells* or *myeloplaxes* of Robin (fig. 54, *meg*; fig. 55). Giant-cells are especially numerous wherever bone is becoming absorbed, but are not confined to such situations, being normal constituents of adult red marrow. Sometimes they possess several nuclei, but most—the so-called *megakaryocytes*—contain but one large nucleus,

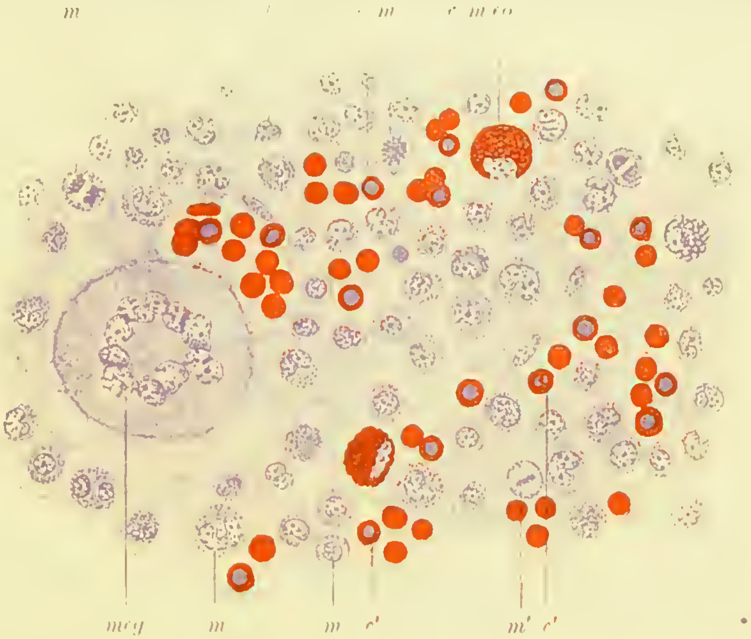

FIG. 54.—RED MARROW OF YOUNG RABBIT. Magnified 450 diameters.

e, erythrocytes; *e'*, erythroblasts; *e''*, a coloured cell undergoing mitotic division; *l*, a polymorph leucocyte; *m*, ordinary myelocytes; *m'*, myelocytes undergoing mitotic division; *eo*, an eosinophil myelocyte; *b*, a basiphil myelocyte; *meg*, a giant-cell or megakaryocyte.

which has usually an annular form, is lobulated, and contains a number of nucleoli. They are also characterised by possessing a number of centrioles grouped together near the centre. Giant-cells are found in all blood-forming organs, *e.g.*, the lymph-glands and spleen, as well as in bone-marrow. Under pathological conditions they may occur in many other tissues.

The existence of cells within the marrow containing blood-corpuscles in various stages of transformation into pigment, similar to those which occur in the spleen-pulp, has been noted by Osler and others.

The marrow is very vascular, the capillaries and veins being large and thin-walled; indeed, according to some authorities, the walls of the capillaries are imperfect, so that there is an open communication between them and the interstices of the tissue, and in this way it is supposed that the coloured blood-disks which are produced from the erythroblasts of the marrow may get into the circulation. There is not, however, an interstitial circulation of blood in the marrow such as is found in the spleen, nor does injection material such as carmine gelatine pass into the interspaces of the tissue; but it remains confined to the vessels, so that the existence of an open communication is improbable.

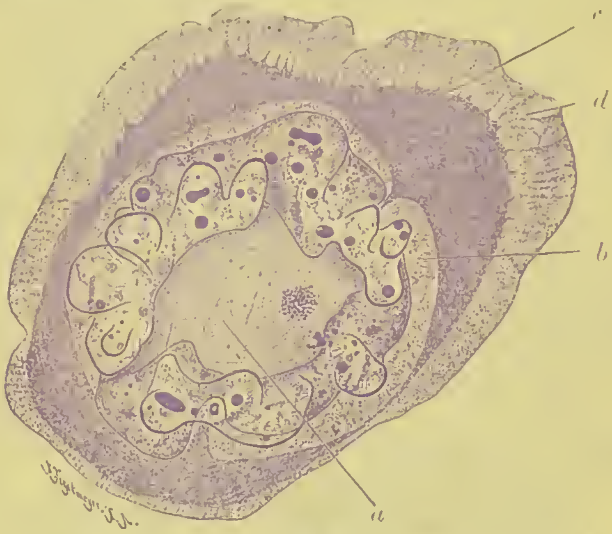

FIG. 55.—GIANT-CELL OF MARROW (RABBIT) WITH ANNULAR NUCLEUS AND NUMEROUS CENTRIOLES. (M. Heidenhain.)

a, *b*, *c*, *d*, zones in protoplasm.

Development of white corpuscles.—The *white blood- and lymph-corpuscles* occur originally as free mesenchyme cells, and are believed to find their way into the vessels from the circumjacent mesoderm. Some authorities state that they are produced by division of the primitive blood-cells, some of these forming primitive lymphocytes, others primitive erythroblasts. According to other authors they do not occur within the first-formed blood-vessels of the embryo. They are not seen within the vasoformative cells. In later stages of fœtal life and during the whole of post-embryonic life they become formed in the bone-marrow, as well as in lymph-glands, in the Malpighian corpuscles of the spleen, and in other organs composed of lymphoid tissue; they pass from these directly into the lymphatics and into the blood.

It is regarded as probable, but has not been ascertained with certainty, that the macrocytes are formed by enlargement of the lymphocytes. Some authors believe that the lymphocytes give origin to all the various kinds of leucocytes. Others, on the other hand, consider that the polymorphs and the coarsely granular oxyphil leucocytes are formed within the bone-marrow, which contains cells of similar character. Leucocytes with well-marked basiphil granules are also met with in bone-marrow; these sometimes, under abnormal conditions, pass in large numbers into the blood, which normally does not contain any such cells.

LESSON IV.

ACTION OF REAGENTS UPON THE HUMAN BLOOD-CORPUSCLES.

1. MAKE a preparation of human blood, and apply a drop of water at one edge of the cover-glass. Examine at a place where the two fluids are becoming mixed. Notice particularly the first effect of water upon both red and white corpuscles, as well as the ultimate action.

Sketch both kinds of corpuscles under the action of water.

2. Repeat on another preparation, using very dilute alkali (0·2 per cent. caustic potash) instead of water. Notice the complete solution first of the white and then of the coloured corpuscles as the alkali reaches them.

3. Repeat on another preparation, using dilute acetic acid (1 per cent.). Observe that the effect of the acid upon the coloured corpuscles is similar to that of water, but that it has a different action upon the colourless corpuscles.

Sketch two or three of the latter after the action is completed.

4. Make a preparation of blood mixed with salt solution, as in Lesson II. 2, and investigate the action of tannic acid (1 part tannic acid to 100 of distilled water) in the same way.

Sketch two or three coloured corpuscles after the action is complete.

5. Examine blood-crystals of rat, guinea-pig, and squirrel. Preparations of hæmoglobin crystals cannot be kept permanently.

6. Prepare hæmin by heating a dry smear of blood on a slide with glacial acetic acid. It is not necessary to add salt since this is present in the blood. The crystals of hæmin are permanent.

Structure of erythrocytes.—The action of reagents upon the human red blood-corpuscles shows that, although to all appearance homogeneous, they in reality consist of an external envelope of colourless material which forms a thin film inclosing the dissolved coloured matter or *hæmoglobin.* Thus, when water reaches the corpuscle, it passes through the film and swells the corpuscle, causing it to become globular; eventually the film is burst, or is sufficiently distended to allow the solution of hæmoglobin to escape through its pores, the colourless envelope (the so-called *stroma*) being left (fig. 56, *a* to *e*). The addition of hyperisotonic solution fo salt, on the other hand, by increasing

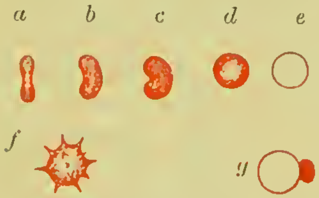

FIG. 56.

a-e, successive effects of water upon a red corpuscle; *f*, effect of solution of salt; *g*, effect of tannic acid.

the density of the fluid in which the corpuscles float, causes diffusion of water out of the corpuscle, and consequent shrinking and corrugation of the surface, the crenated form (fig. 56, *f*) being thereby produced. The same change is brought about by evaporation of water, if the blood is exposed to air. The separation of hæmoglobin from the corpuscle can be effected not only by water, but also by dilute acids, by the action of heat (60° C.), the freezing and thawing of blood, the action of ether or chloroform, and the passage of electric shocks. Bile and dilute alkalies rapidly cause the red corpuscles to become spherical and then almost instantly effect their complete solution (hæmolysis). The mixing of blood from one species of animal with the blood or serum of animals of other species frequently also has a similar effect. In this case the hæmolytic action is exerted by some constituent (hæmolysin) of the foreign blood, which is special for each species and against which the "host" can render itself immune if, prior to any large quantity of the foreign blood or serum being injected, successive small injections be made; an "anti-hæmolysin" being gradually produced. This fact is not only of interest as bearing upon the general doctrine of immunity, but also serves to detect the source of a given sample of blood.

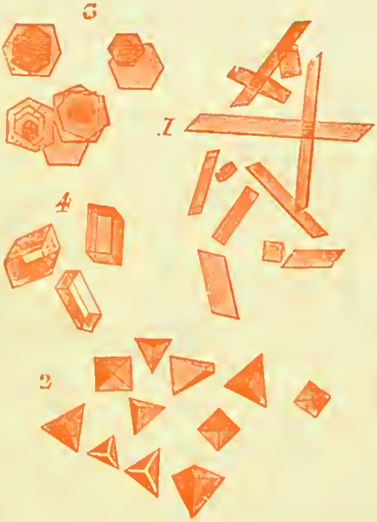

Fig. 57.—Blood crystals, magnified.
1, from human blood; 2, from the guinea-pig; 3, squirrel; 4, hamster

Tannic acid produces a peculiar effect upon the red corpuscles (fig. 56, *g*); the hæmoglobin is discharged from the corpuscle, but is immediately altered and precipitated, remaining adherent to the envelope in the form of a round or irregular globule of a brownish tinge (hæmatin?).

Some of these reactions occur by a process of osmosis as in the case of water, but in others a solution of the envelope of the corpuscle is produced by the reagent, and the hæmoglobin is thus allowed to escape. The film or envelope is probably composed of protoplasm, containing, besides nucleo-proteids, lipoids; and these are substances which possess many of the physical properties of fats, although of a different chemical composition. If we assume that these substances form an external film to the corpuscle, the running of the red disks into rouleaux can readily be explained, since it has been shown by Norris that disks of any material, *e.g.* cork, suspended in a fluid, tend in the same way to adhere in rouleaux, provided their surfaces are covered with a layer which is not wetted by the fluid. We may also explain on the same hypothesis the fact that no rent is ever seen in the envelopes of the red corpuscles even when they appear to have burst, for, if the film which represents an envelope is of a fatty nature, any rent in it would tend immediately to close up again when the opposed edges come in contact.

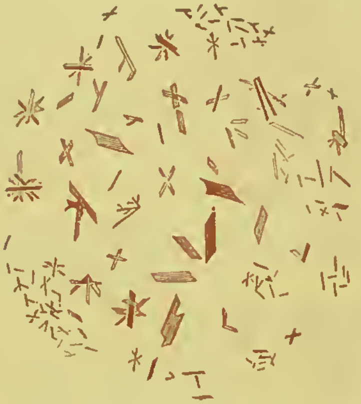

FIG. 58.—HÆMIN CRYSTALS, MAGNIFIED. (Preyer.)

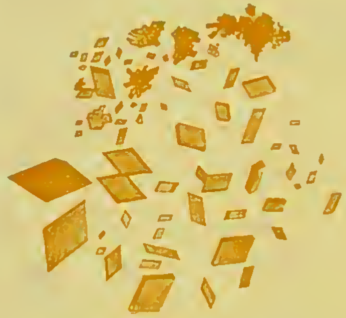

FIG. 59.—HÆMATOIDIN CRYSTALS. (Frey.)

It was also shown by Norris that droplets of fluid encompassed by myelin have a tendency to assume a flattened shape; thus offering an explanation of the flattened form of the erythrocyte.

The more solid part of the erythrocyte is often termed the *stroma*, a name which rests upon a false conception of the structure of the corpuscle. In adopting the name, it was supposed that the corpuscle is formed of a homogeneous porous material (stroma—Rollett), in the pores of which the hæmoglobin is contained, but there is no reasonable foundation for this belief, which fails to explain the well-known osmotic phenomena of the corpuscle; whereas the supposition that there exists an external film or envelope enclosing a coloured fluid is in accordance with all the known facts regarding the action of reagents upon these bodies. It is true that in the fresh mammalian corpuscle the envelope is too delicate to be actually observed in the optical section of the corpuscle, but in the blood-corpuscles of amphibia it can be quite distinctly seen, and with any slight increase in density of the plasma it tends to become wrinkled and the creases in it are plainly visible. In these corpuscles also the nucleus becomes readily displaced, in drawn blood, from its position in the centre of the corpuscle and may lie quite at the side (fig. 69); this is a clear indication of the fluid nature of the contents of the corpuscle, and by analogy we may fairly assume a similar constitution for the mammalian corpuscle. Lastly, it is possible to stain the envelope of the red corpuscles of a different colour from the remainder of the corpuscle.

Blood-crystals—Hæmoglobin.—In the blood of many animals (fig. 57), crystals of hæmoglobin readily form after its separation from the red corpuscles. These crystals are rhombic prisms in man and most animals, *e.g.* the rat, but tetrahedra in the guinea-pig, and hexagonal plates in the squirrel. In these animals they at once appear on shaking up the blood with chloroform or ether, or even on the addition of water, with or without subsequent evaporation.

Hæmin.—This name has been applied to the minute dark-brown rhombic crystals of hydrochlorate of hæmatin (fig. 58), which are formed when dried blood from any source whatever is heated with glacial acetic acid.

Hæmatoidin.—This occurs in the form of brownish-yellow crystals (fig. 59). It is found in old blood extravasations and in other places where blood-corpuscles are undergoing disintegration within the tissues.

Action of reagents on leucocytes.—The structure of the colourless corpuscles is also brought out by the action of some of the reagents above noticed. As the water reaches them their amœboid movements cease; they become swollen out into a globular form by imbibition of fluid (fig. 60, 1), and the granules within the protoplasm can be seen to be in active Brownian motion. Their nuclei also become clear and globular, and are more conspicuous than before. With the further action of the water, the corpuscle is disintegrated and the granules are set free.

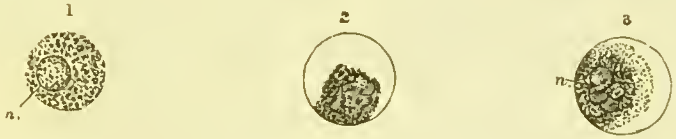

FIG. 60.

1, first effect of the action of water upon a white blood-corpuscle; 2, 3, white corpuscles treated with dilute acetic acid; *n*, nucleus.

Acids have an entirely different action upon the white corpuscles. Their nuclei become somewhat shrunken and very distinct (fig. 60, 2 and 3), and a granular precipitate is formed in the protoplasm around the nucleus. At the same time, a part of the protoplasm generally swells out so as to form a clear bleb-like expansion (an appearance which also often accompanies the death of the corpuscle from other causes). Caustic alkalies, even when very dilute, rapidly cause the complete destruction of the white corpuscles.

LESSON V.

THE BLOOD-CORPUSCLES OF AMPHIBIA.

1. Obtain a drop of frog's, toad's or newt's blood, and mix it with a very small quantity of normal salt solution upon a slide. Examine with the high power. Notice the shape of the coloured corpuscles both when seen flat and edgeways, and the nucleus within each.

Measure ten corpuscles (long and short diameters), and from the results obtain the average dimensions of a corpuscle.

Notice also the colourless corpuscles, smaller than the red, but larger than the pale corpuscles of human blood, although otherwise generally resembling these. Spindle-shaped blood-platelets may also be seen.

Sketch two or three red corpuscles and as many white.

Be careful not to mistake the rounded liberated nuclei of crushed red corpuscles for pale corpuscles.

Enormous cells and nuclei belonging to the cutaneous glands as well as the granular secretion of those glands may be present in this preparation if it is obtained from the newt's tail.

2. Apply a drop of water to the edge of the cover-glass of the same preparation and notice its action upon the corpuscles.

Sketch two or three corpuscles altered by the action of the water.

3. Mount another drop of blood, and apply dilute acetic acid (1 per cent.) instead of water at the edge of the cover-glass. Make sketches showing the effect of the acid upon both red and white corpuscles.

4. Examine the corpuscles of newt's blood which has been allowed to flow into boric acid solution (2 per cent.). Notice the effect produced upon the coloured corpuscles. Sketch one or two.

5. Mount drops of glycerine-jelly containing (*a*) frog's or newt's blood and (*b*) bird's blood, previously fixed by Flemming's solution and stained with picro-carmine.

6. Make a film preparation of amphibian or avine blood as described on pp. 30-32, § 5 for human blood.

The **coloured blood-corpuscles of amphibia** (figs. 61, 62), as well as of nearly all vertebrates below mammals, are biconvex elliptical disks, considerably larger than the biconcave circular disks of mammals.[1] In addition to the coloured body of the corpuscle, which consists,

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[1] The following are the dimensions in parts of a millimeter of the coloured corpuscles of some oviparous vertebrates:—

	Long Diameter.	Short Diameter.
Pigeon,	0·0147	0·0065
Frog,	0·0223	0·0157
Newt,	0·0293	0·0195
Proteus,	0·0580	0·0350
Amphiuma.	0·0770	0·0460

as in mammals, of hæmoglobin inclosed within an envelope, there is a colourless *nucleus*, also of an elliptical shape, but easily becoming globular, especially if liberated by any means from the corpuscle.

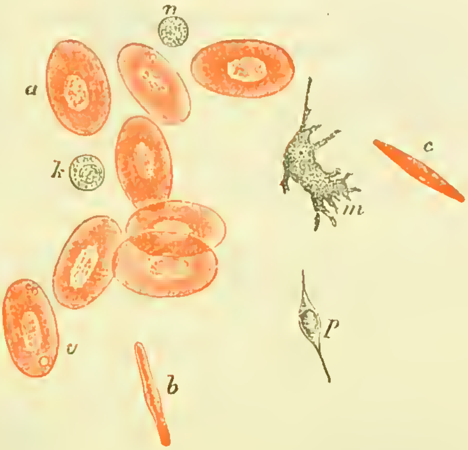

Fig. 61.—Blood-corpuscles of frog. (Ranvier.)

a, seen on the flat; *b*, in optical section; *c*, in profile; *v*, a corpuscle with apparent vacuoles (probably parasitic organisms which are common in frog's blood-corpuscles); *m*, an amœboid leucocyte; *n*, a nucleus of an erythrocyte, set free and contracted to a spherical form; *k*, a lymphocyte; *p*, a blood-platelet.

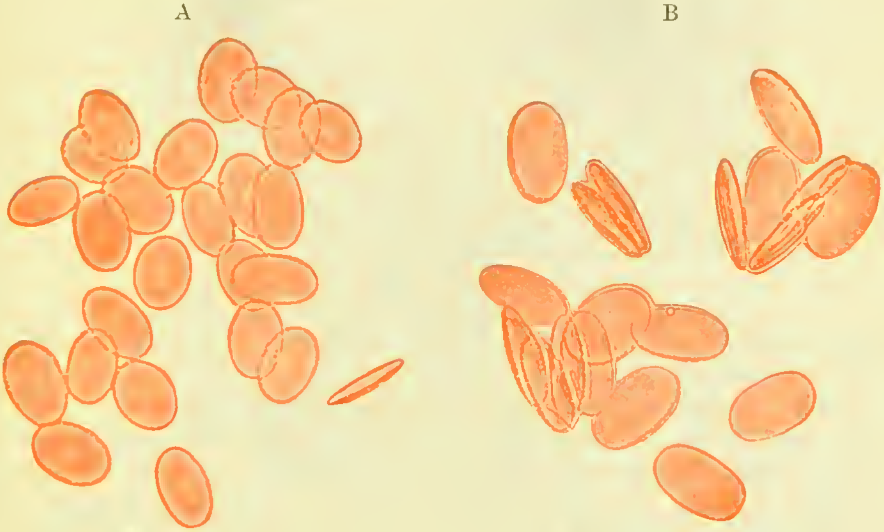

Fig. 62—Amphibian erythrocytes. (From photographs.) Magnified 450 diameters.

A, from the frog. B, from the toad.

The nucleus resembles that of other cells in structure, being bounded by a membrane and having a network of chromatin. It is not very distinct in the unaltered corpuscle, but is brought clearly into view by the action of reagents, especially acids. The action of reagents upon the red corpuscle of amphibia is otherwise similar to that upon the mammalian corpuscle, water and acetic acid causing it to swell into a globular form and then to become decolorised; solution of salt causing wrinkling of the envelope, and so on. As a first effect, water and certain other fluids may cause the hæmoglobin to retire from the envelope at the points where the fluid is passing through the membrane: a stellate appearance is thereby often produced. Boric acid causes the hæmoglobin of the newt's corpuscle to become partially or wholly collected around the nucleus, which may then be extruded from the corpuscle.

Immediately within the envelope, at the periphery of the amphibian erythrocyte, is a band of fine fibrils which are stained by gentian violet (Meves) and can also be seen cut across in sections of the corpuscles (Bryce) (fig. 63).

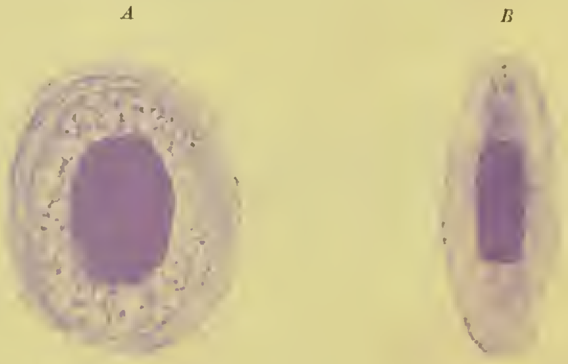

FIG. 63.—ERYTHROCYTES OF LEPIDOSIREN LARVA, FIXED WITH FLEMMING'S SOLUTION AND STAINED WITH IRON-HÆMATOXYLIN. (T. H. Bryce.)

A, as seen on the flat; *B*, in section. In *A* the fibrils around the edge are visible as fine lines parallel to the margin of the corpuscle. In *B* their sections are seen as fine points just within the thinnest part of the edge.

The colourless corpuscles of amphibia, although larger, are very similar to those of mammals. Like them, they are either wholly pale and finely granular, or inclose a number of very distinct granules of similar nature to those met with in mammals. These corpuscles vary much in size and in the activity of their amœboid movements: those which have a multilobular nucleus (fig. 67) are usually the most active. Reagents have the same effect upon the amphibian leucocytes as on those of mammals. The presence of glycogen may be demonstrated in them by its reaction with iodine (port-wine colour).

The **blood-platelets** (thrombocytes) in the frog are fewer in number than in mammals. Many are of a spindle shape (fig. 61, *p*). They contain a nucleus-like body, and like the blood-platelets of mammals they show rapid changes as soon as the blood is drawn. These changes are represented in the accompanying figures (figs. 64 and 65) from Meves. The elongated corpuscle first contracts and becomes more or less globular, its nucleus also changing similarly in shape. Amœboid processes begin to be protruded, and then fine threads are shot out radially in all directions, these becoming attached to those of other platelets, or to any solid object which may be in the vicinity of the

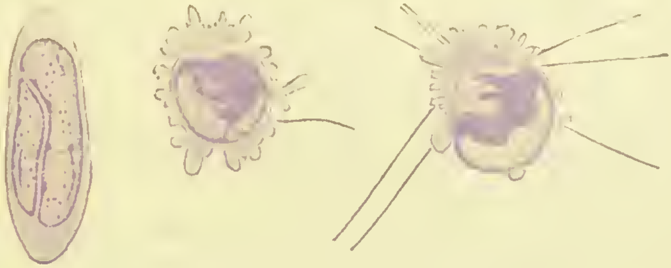

FIG. 64.—A BLOOD-PLATELET OF SALAMANDRA, AND THE CHANGES WHICH IT UNDERWENT IMMEDIATELY AFTER WITHDRAWAL OF BLOOD FROM THE VESSELS. (F. Meves.)

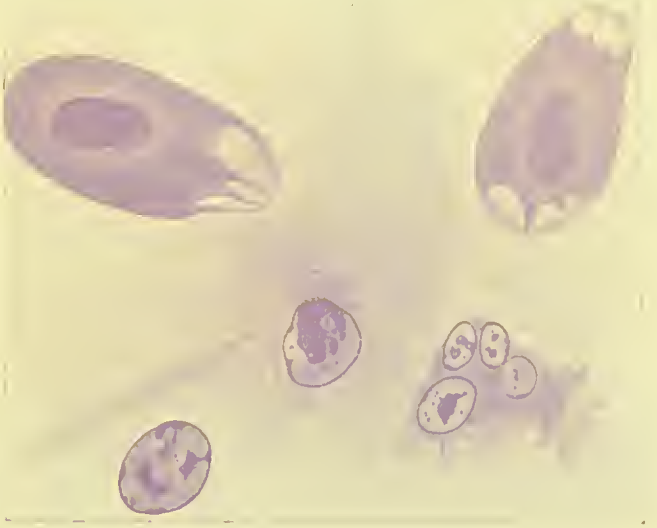

FIG. 65.—A BLOOD-PLATELET OF SALAMANDRA, SHOWING ITS AMŒBOID PROJECTIONS AND THE FIBRINOUS FILAMENTS RADIATING FROM IT AND ATTACHED TO ADJACENT BLOOD-CORPUSCLES. (F. Meves.)

Two erythrocytes, one free nucleus, and one polymorph leucocyte are included in the figure.

platelet. The filaments, which appear to be of a fibrinous nature, and may possibly be threads of fibrin, then begin to retract and drag upon the objects which may be entangled by them. In this manner a number of erythrocytes may be drawn together towards a common centre and assume a more or less radial arrangement. Probably similar changes occur in the blood-platelets of mammalian blood. It is believed that the entanglement of blood-platelets and other corpuscles may serve rapidly to plug small apertures in blood-vessels caused by injury, and thus serve to aid in arresting hæmorrhage.

Corpuscles having a similar character and fulfilling similar functions have been also noticed in the blood of invertebrates (Geddes, Tait).

LESSON VI.

THE AMŒBOID PHENOMENA OF THE COLOURLESS BLOOD-CORPUSCLES.

1. Make a preparation of blood from the finger in the usual way. Draw a brush just moistened with thick paraffin oil around the edge of the cover-glass to check evaporation. Avoid an excess of oil. Place the preparation upon a 'warm stage,' and heat this to about the temperature of the body (38° C.). Bring a white corpuscle under observation with the high power, and watch the changes of shape which it undergoes. To become convinced of these alterations in form, make a series of outline sketches of the same corpuscle at intervals of a minute.

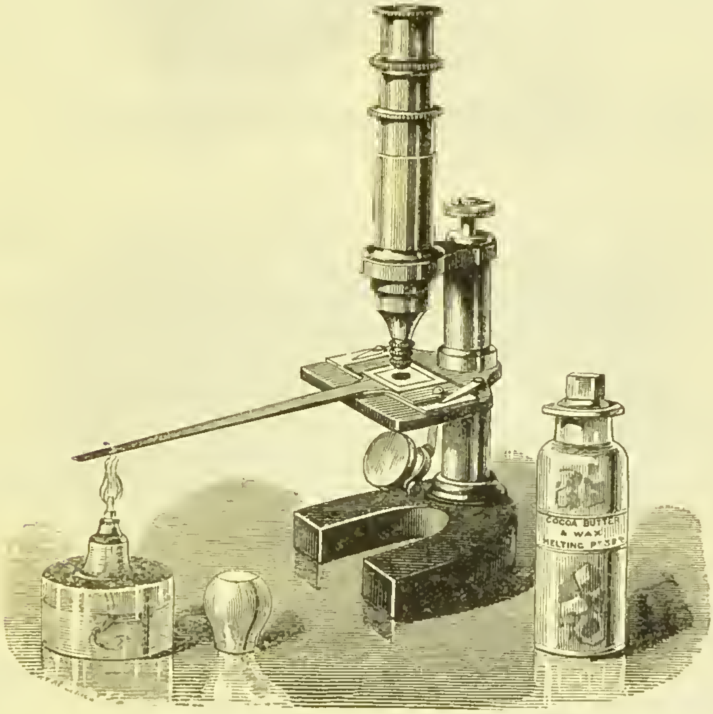

Fig. 66.—Simple warming apparatus, complete, shown in operation.

The simplest form of warm stage is a copper plate of about the size of an ordinary slide, perforated in the centre and with a long tongue of the same metal projecting from the middle of one edge (fig. 66). The copper plate rests upon the stage of the microscope, with a piece of cloth or other non-conducting material between. The preparation is made upon an ordinary slide or on a large cover-glass, which is placed upon the warm stage and pressed into contact with it by the brass clips. Heat is applied to the copper tongue by a small spirit-lamp flame, and a greater or less amount is conducted to the warm stage and the superjacent preparation according to the point to which the flame is applied. To ascertain that the right temperature is got and maintained, put two pieces of solid paraffin, one melting at 35° C. (95° F.) and another at 38° C. (100° F.), on either side of the preparation. The temperature must be such that the first piece is melted and remains so whilst the second remains unmelted.[1]

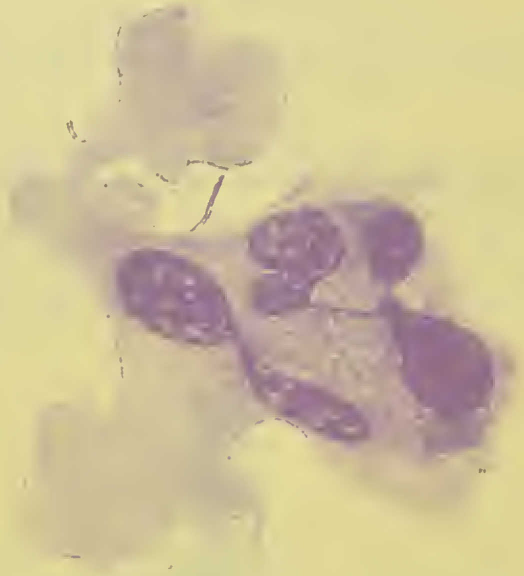

FIG. 67.—A POLYMORPH LEUCOCYTE OF TRITON FIXED BY STEAM IN AMŒBOID CONDITION AND STAINED WITH HÆMATOXYLIN. Untouched photograph. Magnified 1360 diameters.

Notice the homogeneous appearance of the protoplasm of the pseudopodia as compared with that of the body of the corpuscle. The nucleus is multilobed, the lobes being joined by threads of chromatin. Its reticular structure is well shown.

2. Mount a drop of frog's or newt's blood diluted with an equal amount of salt solution, and examine it in the same manner upon the copper stage, at first cold, afterwards warm; the temperature must, however, be kept below 30° C. Observe the effect of warmth in accelerating the amœboid movements of the pale corpuscles. Sketch one at intervals of a minute (*a*) in the cold, (*b*) whilst warmed.

3. Take some yeast which has been mixed with salt solution, and mix a very little of the yeast and salt solution with a fresh drop of newt's blood, slightly oiling the edge of the cover-glass as before. Endeavour to observe the inception of the yeast-torulæ by the white corpuscles. Sketch one or two corpuscles containing torulæ.

Milk-globules or particles of carbon or of vermilion may also be used for this experiment, but the process of 'feeding' is most readily observed with the yeast particles.

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[1] For exact work, an apparatus somewhat more complex than the above is required. For description of such apparatus, see the author's *Course of Practical Histology*.

4. At the beginning of the lesson collect a drop of newt's or frog's blood into a very fine capillary tube, seal the ends of the tube, and mount it in a drop of oil of cedar-wood or dammar varnish (or the clot may be blown out into a drop of salt solution on a slide and mounted in this solution). Towards the end of the lesson examine it to see white corpuscles emigrating from the shrunken clot (fig. 68).

5. To obtain a specimen with the white corpuscles fixed in amœboid condition, make a preparation of newt's blood, mixed with salt solution, and set it aside for ten minutes. By this time the corpuscles will be freely amœboid, and will probably show well-marked pseudopodia. To fix them in this condition let a jet of steam from a tube attached to a boiling flask or kettle of water play for a second or two seconds upon the cover-glass. The heat instantly kills the corpuscles, and they are fixed in the form they presented at the moment the steam was applied. They may now be stained by passing dilute hæmalum[1] under the cover-glass, or by removing the latter and staining with eosin and methylene blue in the manner recommended for blood films. If hæmalum is used, the stain is followed by dilute glycerine, after which the cover may be cemented and the preparation kept.

The **amœboid phenomena** which are exhibited by the protoplasm of the colourless blood-corpuscles consist of spontaneous changes of form, produced by the throwing out of processes or *pseudopodia* in various directions. When first thrown out the pseudopodia are quite clear; they appear to be produced by a flowing of the hyaloplasm (see p. 4). If the corpuscle is stimulated, either mechanically, as by

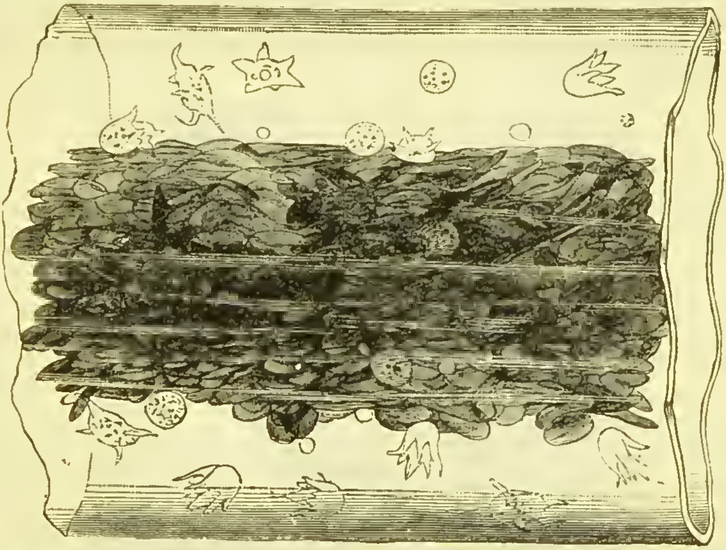

FIG. 68.—WHITE CORPUSCLES OF FROG'S BLOOD MIGRATING FROM SHRUNKEN CLOT WITHIN A CAPILLARY TUBE.

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[1] Delafield's or Ehrlich's hæmatoxylin can be substituted for hæmalum wherever the latter is mentioned. The water used for the dilution of hæmatoxylin solutions must always be distilled.

tapping the cover-glass, or electrically, the pseudopodia are retracted, the corpuscles becoming spherical. A change of form caused by the protrusion of the pseudopodia may, when active, be followed by

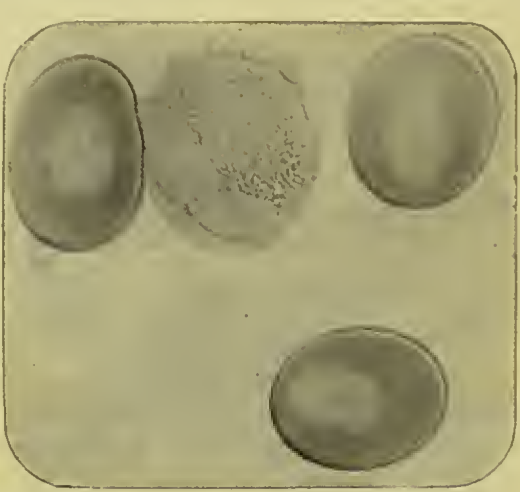

FIG. 69.—AN EOSINOPHIL LEUCOCYTE OF SALAMANDRA BEGINNING TO ADHERE TO AN ERYTHROCYTE. Fresh preparation without addition of fluid. Untouched photograph. Magnified 600 diameters.

Two other erythrocytes are included in the field. Notice that the nuclei in these have undergone a change of position within the corpuscle, showing that its contents must be completely fluid.

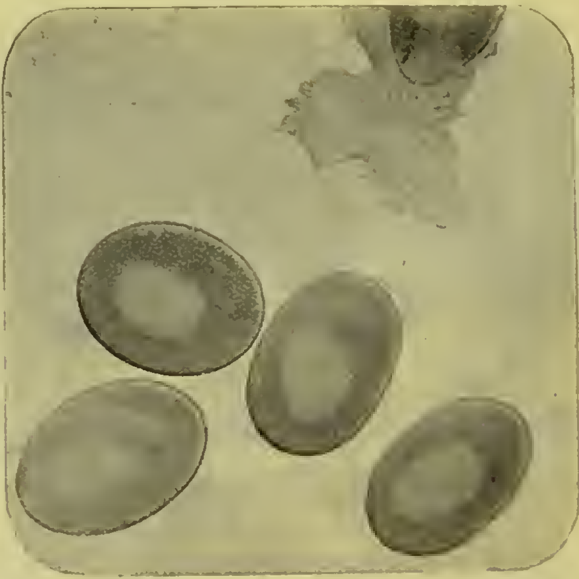

FIG. 70.—A HIGHLY AMŒBOID PHAGOCYTIC POLYMORPH LEUCOCYTE OF SALAMANDRA, ENVELOPING AN ERYTHROCYTE (a portion only of this is included in the field). Untouched instantaneous photograph. Magnified 600 diameters.

Four other erythrocytes are represented.

changes in place or actual locomotion (migration) of the corpuscle (fig. 68) When a pseudopodium, or the external surface of the corpuscle, comes in contact with any foreign body, the protoplasm tends to flow round and enwrap it and it is then drawn into the corpuscle (figs. 69, 70) ; particles thus incepted may be conveyed by the corpuscle in its movements from one place to another (fig. 71). This property plays an important part in many physiological and pathological processes ; thus cells in the spleen resembling large leucocytes—the so-called *splenic cells*—incept blood-corpuscles, which become broken down within them ; and pathogenic bacteria become taken into the protoplasm of certain leucocytes (on this account termed *phagocytes*), there to be destroyed (Metchnikoff). The phagocytic properties of the leucocytes become especially developed as the result of the action upon the bacteria of certain chemical substances which are present to a greater or less extent in blood and which are termed *opsonins* (Wright).

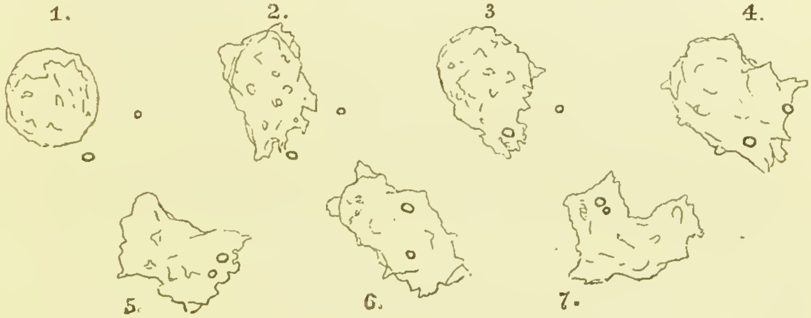

FIG. 71.—CHANGES OF FORM OF A WHITE BLOOD-CORPUSCLE SKETCHED AT INTERVALS OF A FEW MINUTES, SHOWING THE INCEPTION OF TWO SMALL GRANULES AND THE CHANGES OF POSITION THESE UNDERWENT WITHIN THE CORPUSCLE.

It is probable that particles of organic matter which are taken up by the pale corpuscles may undergo some slow process of intracellular digestion within their protoplasm.

The processes of the granular corpuscles are quite clear at first ; the granules afterwards flow into them.

The migration of the colourless corpuscles from the blood-vessels into the surrounding tissues (which especially occurs in inflamed parts), or from a blood-clot into the surrounding serum (fig. 68), is due to these amœboid properties.

The conditions which are favourable to this amœboid activity of the white corpuscles are (1) the natural slightly alkaline medium, such as plasma, serum, or lymph, or faintly alkaline normal saline solution. Any increase of density of the medium produces a diminution of amœboid activity, whilst, on the other hand, a slight decrease in its density has the opposite effect; (2) a certain temperature. In warm-blooded animals the phenomena cease below about 10° C. When gradually warmed the white corpuscles become more and more active up to a certain point, the maximum being a few degrees above the natural temperature of the blood. Above this point they become spheroidal and at a somewhat higher temperature their protoplasm is coagulated and killed. Acids at once kill the corpuscles and stop the movements. Narcotic gases and vapours, such as carbonic acid gas or chloroform vapour, also arrest the movement, but it recommences after a time if their action is not too prolonged.

LESSON VII.

EPITHELIUM AND SECRETING GLANDS.

1. Mount a drop of saliva and examine first with a low, afterwards with a high power. Observe the nucleated epithelium-cells, some single, and others still adhering together by overlapping edges. Measure three or four, and also their nuclei. Sketch one or two on the flat and one edgeways. Notice the salivary corpuscles, which are migrated white blood-corpuscles swollen out by imbibition of water. The preparation may be stained with diluted hæmalum and preserved with glycerine.

2. Put a small shred of human epidermis into a drop of strong caustic potash solution (35 p.c.) for five minutes. Then break it up in water with needles, cover and examine. Observe the now isolated swollen cells.

3. Study the arrangement of the cells in a section through some stratified epithelium, such as that of the mouth, skin, or cornea.[1] Notice the changes in shape of the cells as they are traced towards the free surface. Measure the thickness of the epithelium. Count the number of layers of cells.

4. Make a preparation of the epithelium of the urinary bladder, which may be moderately distended with bichromate of potash solution (1 part to 800 of salt solution), and after an hour or two cut open and placed in more of the same solution. Take a small scraping of the lining epithelium on the point of a scalpel, and break it up by tapping it in a drop of *very dilute* hæmatoxylin on a slide. Put a small hair in the drop and cover. Add a *small drop* of glycerine at one edge: allow this to diffuse under. Cement next day. Observe the large flat superficial cells, and the pear-shaped cells of the second layer. Sketch one of each kind. The cells will vary greatly in appearance according to the amount of distension of the organ.

5. Study the minute structure of epithelium-cells and their nuclei, both at rest and dividing, in sections of the skin of the newt's tail, or in shreds of peritoneum or of the amnion of the rat, or in sections of the salamander-tadpole. The preparation may, for this purpose, be stained either with hæmatoxylin or iron-hæmatoxylin, or with some aniline dye such as saffranin.[1]

Sketch a cell with resting nucleus, and others with nuclei in different phases of mitosis.

The simpler saccular skin-glands of Amphibia may also be studied in preparations from the newt's tail.

An **epithelium** is a tissue composed entirely of cells separated by a very small amount of intercellular substance (cement-substance) and generally arranged so as to form a membrane covering either an external or internal free surface.

The structure of epithelium-cells, and the changes which they undergo in cell-division, are best seen in the epidermis of the newt or of the salamander-tadpole (fig. 72); in the latter especially, the cells and nuclei are much larger than in mammals.

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[1] The methods of preparing and staining are given in the Appendix.

Structure of the cells.—Each epithelium-cell consists of *protoplasm* containing a *nucleus*. The protoplasm may either look granular, or it may have a reticulated appearance, or may exhibit fibrils. The nucleus is spherical or ovoid. Usually there is only one, but there may be two or more. The cell-substance is often modified in its chemical nature; its external layer may become hardened to form a sort of membrane, or the whole cell may become horny (keratinised); or there may be a separation of materials (granules) within the cell which are ultimately used by the organism, as in some secreting glands.

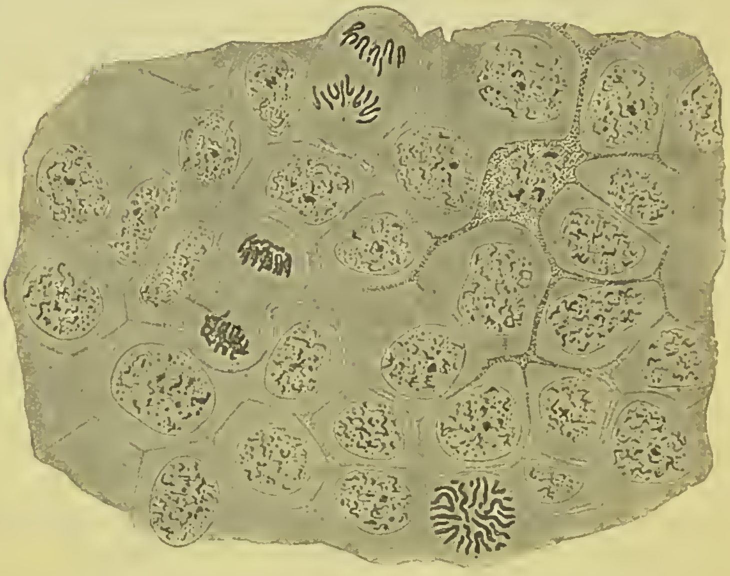

FIG. 72.—EPIDERMIS CELLS OF A LARVAL SALAMANDER. Magnified 400 diameters. (Wilson.)

Three of the cells are undergoing division. The intercellular channels are bridged across by fine fibres. At one place a branched pigment cell is lying between the epithelium cells.

Classification of epithelia.—Epithelia are somewhat illogically classified partly according to the shape and arrangement of the cells, partly according to their function. Thus we speak of *scaly* or *pavement*, *cubical*, *columnar*, *glandular*, and *ciliated* epithelium. Most of these are *simple* epithelia, with the cells only one layer deep. If forming several superposed layers, the epithelium is said to be *stratified*, and then the shape of the cells differs in the different layers. Where there are only three or four layers in an epithelium, it is termed *transitional.* A classification according to the function of the epithelium may also conveniently be adopted. We should then include under the term *protective epithelia*, the pavement, stratified and transitional varieties, under the term *secreting epithelia*, the cubical, columnar[1] and glandular epithelia (some of the pavement epithelia would come also under this head), while the *ciliated epithelia* would form a separate division, as in the classification above given.

Stratified epithelium (fig. 73) covers the anterior surface of the cornea, lines the mouth, pharnyx (lower part), gullet, anal canal and part of the urethra, and forms the epidermis which covers the skin. The vocal cords are covered by stratified epithelium. In the female it also lines the vagina and covers the os uteri. The cells nearest the surface are always flattened and scale-like, whereas the deeper cells are polyhedral, and those of the deepest layer somewhat columnar in shape. Moreover, the deep cells are soft and protoplasmic, and are separated from one another by a system of intercellular channels, which are bridged across by numerous fibrils passing from cell to cell (figs. 74, 75); giving the cells, when separated, the appearance of being beset with short spines (*prickle-cells* of Max Schultze). These 'bridging fibrils' are not peculiar to stratified epithelium, but occur in many if not in all epithelia.

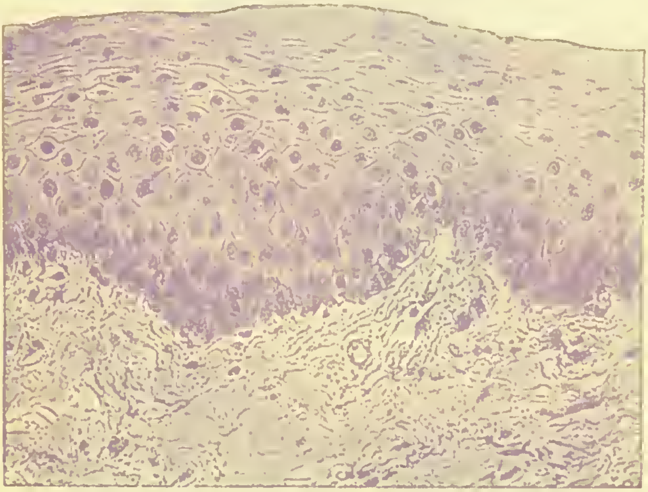

FIG. 73.—SECTION OF THE STRATIFIED EPITHELIUM OF THE FAUCES OF THE RABBIT. Magnified 240 diameters. Photograph.

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[1] The columnar epithelium of the intestine is concerned as much with absorption as with secretion, but absorption may be regarded as a kind of reversed secretion.

The deeper cells multiply by mitotic division, the nuclei first dividing in the manner already described. The newly formed cells tend as they

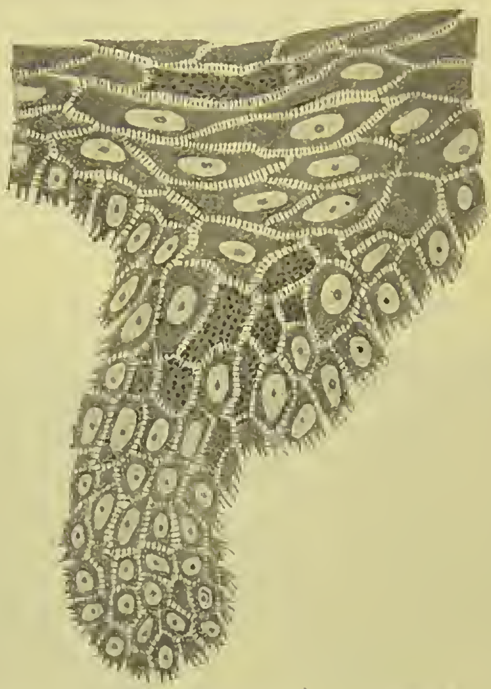

Fig. 74.—Section of epidermis of cat's foot showing intercellular channels, with bridging fibrils. (Kolossow.)

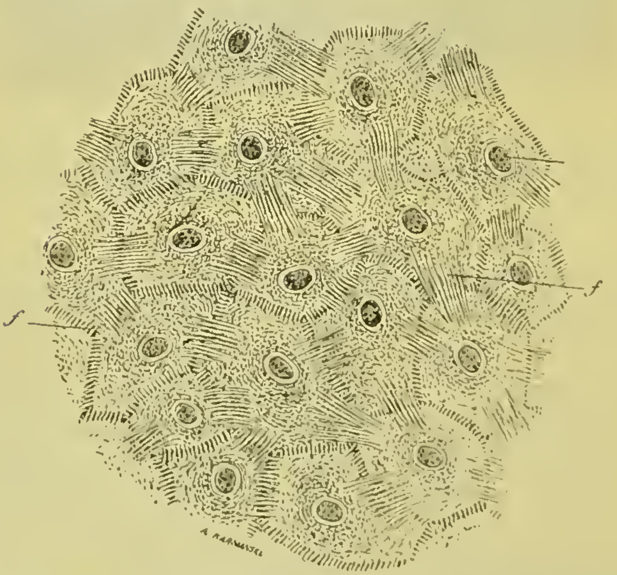

Fig. 75.—Section through the deeper layers of a stratified epithelium, showing fibrils, *f*, passing from cell to cell across the intercellular spaces. (Ranvier.)

enlarge to push those external to them nearer to the surface, from which they are eventually thrown off. As they approach the surface they become hard and horny, and in the case of the epidermis entirely lose their cellular appearance, which can, however, be in a measure restored by the action of alkalies (§ 2). The cast-off superficial cells of the stratified epithelium of the mouth, which are seen in abundance in the saliva (§ 1), are less altered, and the remains of a nucleus is still visible in them (fig. 76). The stratified epithelium of the human skin (epidermis) shows many peculiarities: these will be considered when the skin itself is treated of.

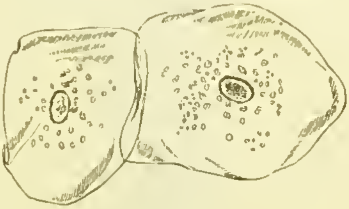

FIG. 76.—EPITHELIUM-SCALES FROM THE INSIDE OF THE MOUTH. (Sharpey.) Magnified 260 diameters.

Transitional epithelium is a stratified epithelium consisting of only three or four layers of cells. It occurs in the urinary bladder, the ureter, and the pelvis of the kidney. The superficial cells (fig. 77, *a*) are large and flattened; they often have two nuclei. Their free surface is covered with a cuticular stratum (Eggeling), and on their under surface they exhibit depressions, into which fit the larger ends of pyriform cells, which form the next layer (fig. 77, *b*). Between the tapered ends of the pyriform cells one or two layers of smaller polyhedral cells are found. The epithelium seems to be renewed by mitotic division of these deeper cells; it is possible that the superficial cells also multiply, but in this case by amitosis.

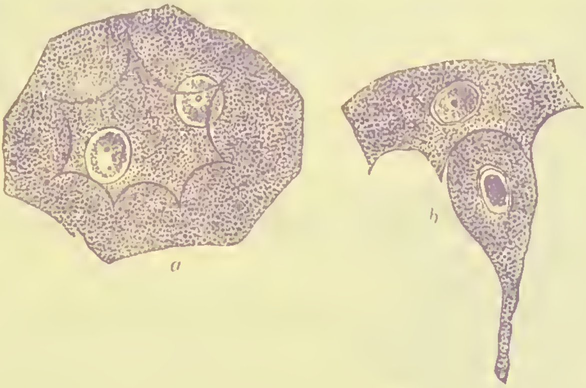

FIG. 77.—EPITHELIAL CELLS FROM THE BLADDER OF THE RABBIT. (Klein.) Magnified 500 diameters.

a, large flattened cell from the superficial layer, with two nuclei and with strongly marked ridges and intervening depressions on its under surface; *b*, pear-shaped cell of the second layer adapted to a depression on one of the superficial cells.

Simple scaly or **pavement epithelium** is found in the saccules of the lungs, in the ducts of the mammary glands, in the kidney (in the tubes of Henle, lining the capsules of the Malpighian bodies, and covering the glomeruli), and also lining the cavities of serous membranes (fig. 78), and the interior of the heart, blood-vessels, and lymphatics. When occurring on internal surfaces, such as those of the serous membranes, blood-vessels, and lymphatics, it is often spoken of as **endothelium** or **mesothelium.** According to v. Brunn the cells of a serous epithelium may be provided with a striated border on their free surface, somewhat like that which is found on columnar cells.

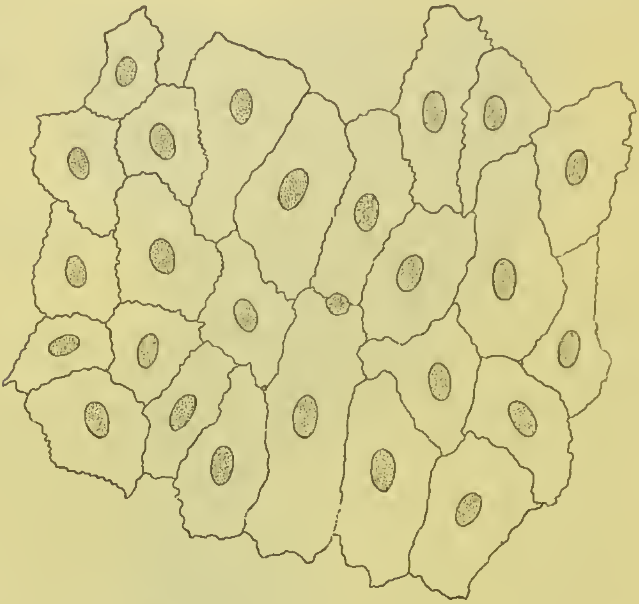

FIG. 78.—PAVEMENT EPITHELIUM OR ENDOTHELIUM OF A SEROUS MEMBRANE. NITRATE OF SILVER PREPARATION. CARMINE STAINING OF NUCLEI.

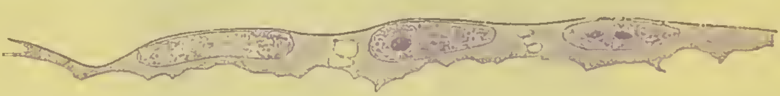

FIG. 79.—ENDOTHELIUM-CELLS OF SEROUS MEMBRANE SEEN IN PROFILE VIEW, SHOWING PROTOPLASMIC BRIDGES STRETCHING ACROSS THE INTERCELLULAR SPACES. (M. Heidenhain.)

GLANDULAR EPITHELIUM AND SECRETING GLANDS.

Glandular epithelium is the essential tissue of all the organs which are known as secreting glands. Glands are of two chief kinds. Those which are best known and which are termed *secreting glands proper* are

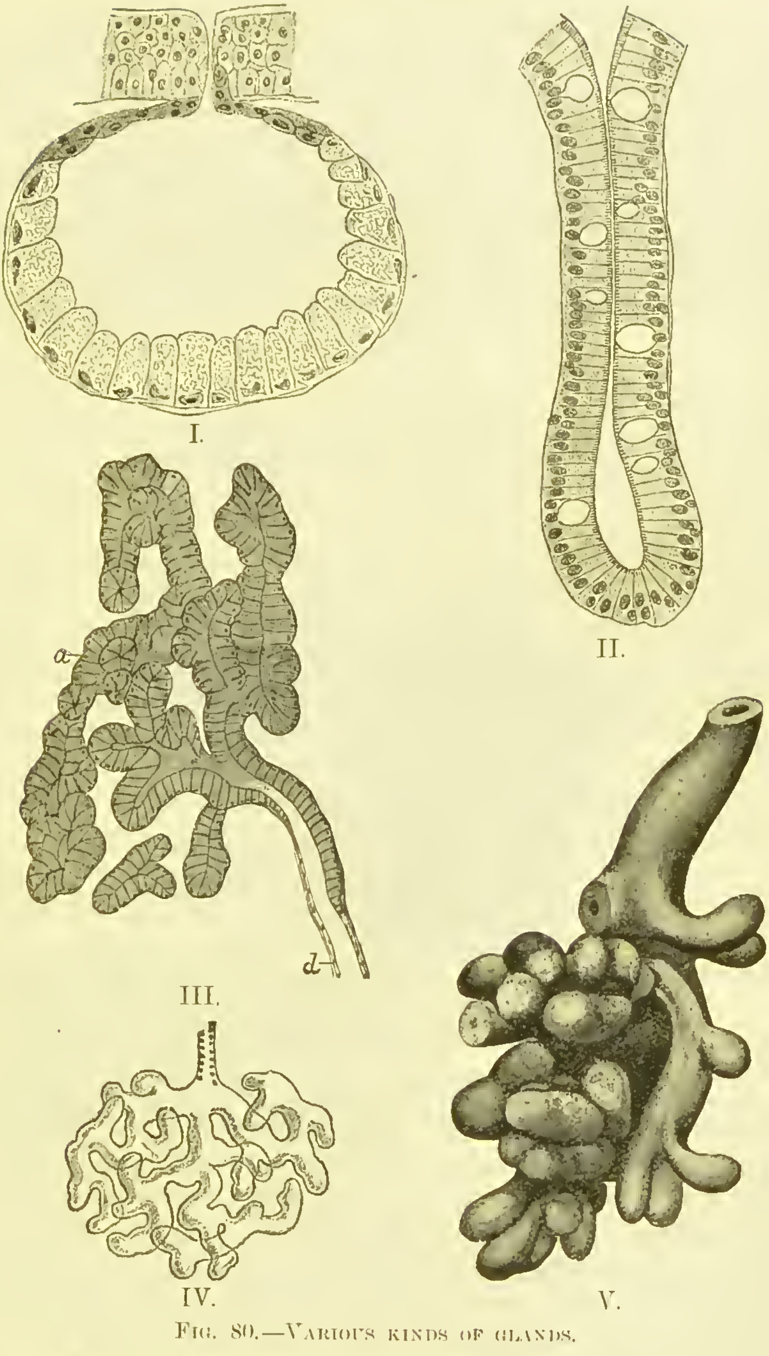

FIG. 80.—VARIOUS KINDS OF GLANDS.

I. Simple saccular gland from amphibian skin (Flemming). II. Simple tubular gland from intestine (Flemming). III. A small racemose gland with a single duct, *d*, into which a number of irregularly tubular acini, *a*, open (Flemming). IV. Part of a tubulo-racemose gland with the acini unravelled (Flemming). V. Wax model of a small tubulo-racemose gland from the epiglottis (Maziarski).

furnished with a duct which ramifies in all parts of the gland and by means of which the products of the secretory activity of the gland-cells are brought to a free surface. Such glands have been developed as involutions of the surface upon which they open, and their epithelium is continuous with that of this surface, and is in some cases, especially where the surface upon which the gland opens is covered with columnar epithelium, of a similar character to the epithelium of the surface; in others different in character. In most glands the epithelium alters as we trace the duct back into the recesses or *alveoli* of the gland, and it is in these that the characteristic glandular cells, which are generally polyhedral in shape, are found. Every such involution or ingrowth of epithelium to form a gland is, when first formed, of a simple character, shaped like a test-tube or flask and filled with a solid mass of cells, but it presently becomes hollowed out and the cells are left as a lining to the connective tissue membrane which bounds the involution. The gland may remain simple and unbranched (*simple saccular* and *simple tubular glands*, fig. 79, I. and II.), or it may branch again and again until a complicated structure, in some cases small, in others of considerable size, is produced (*compound tubular* and *compound saccular* (or *racemose glands*) (fig. 79, III., IV., V.), instances of which are furnished by the kidneys

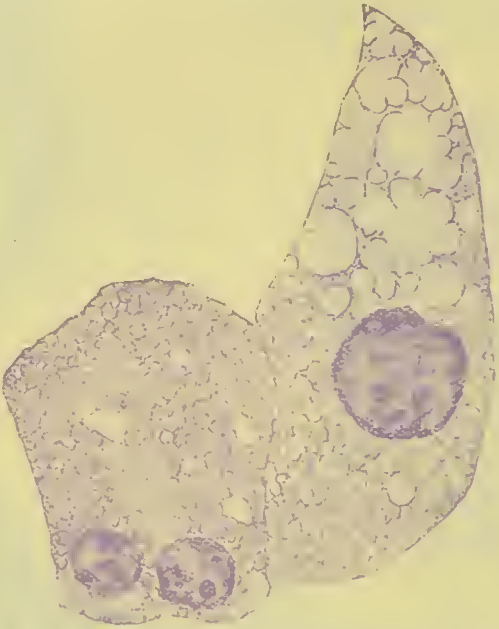

FIG. 81.—TWO CELLS FROM A CUTANEOUS GLAND OF SALAMANDER-LARVA, SHOWING THE SECRETION GRANULES. (Gurwitsch.)

The left-hand cell, which has two nuclei, is filled with granules. In the right-hand cell the granules are becoming swollen and dissolved.

and salivary glands respectively). The cells which furnish the secretion of the gland and which line the secreting parts of the tubules of a tubular gland, or the alveolar enlargements (acini) at the ends of the ducts of a racemose gland, are frequently partly or wholly filled with granules in the intervals of secretory activity, and these granules become discharged or dissolved and pass into the secretion during activity. Secreting glands are always abundantly supplied with blood-vessels and nerves. The former are distributed in the connective tissue which holds together the acini and groups of acini (lobules) of the gland; the latter are supplied partly to the blood-vessels and partly ramify amongst the secretory epithelium cells.

The liver differs from all other secreting glands in being composed of solid masses of cells (hepatic lobules) instead of tubular acini lined by epithelium. It exhibits also other important differences in the nature of its blood-supply and the relation between the blood and the liver-cells.

The other kind of secreting glands, known as the *internally secreting glands*, are not furnished with ducts and are usually described (along with the spleen and the lymphoid structures) as *ductless glands*. The internally secreting glands are, like the externally secreting organs, composed of epithelial cells, sometimes grouped in solid masses (*e.g.* suprarenal gland), in other cases disposed around hollow vesicles (*e.g.* thyroid) which become filled with the material of the secretion. But as in these glands there is no duct the secretion is carried into the blood either directly by the blood-vessels of the gland or indirectly through the lymphatics.

The detailed study of the glands and of other epithelial structures may be reserved until the organs in which they occur are described, but columnar and ciliated epithelia will be dealt with in the next lesson.

The *hairs* and *nails* and the *enamel* of the teeth are modified epithelial tissues. They will be described along with the skin and structures connected with the mouth respectively.

LESSON VIII.

COLUMNAR AND CILIATED EPITHELIUM: ACTION OF CILIA.

1. Break up in dilute glycerine a shred of epithelium from a minute piece of the mucous membrane of intestine (frog) that has been treated with 1 per cent. osmic acid for some hours, and has subsequently macerated in water for a few days. The cells easily separate on tapping the cover-glass. Measure and sketch one or two cells.

The cover-glass may be at once fixed by gold size.

2. Prepare ciliated epithelium from a trachea that has been treated with osmic acid like the last preparation, or that has macerated in chromic acid solution (1 to 2000 normal saline) for a few days. Measure in one or two of the cells (*a*) the length of the cell, (*b*) the length of the cilia, (*c*) the size of the nucleus. Sketch two or three cells.

3. Mount in sea-water one or two bars of the gill of the marine mussel (fig. 82). Study the action of the large cilia. Now place the preparation upon the copper warm stage (see Lesson VI.) and observe the effect of gently raising the temperature.

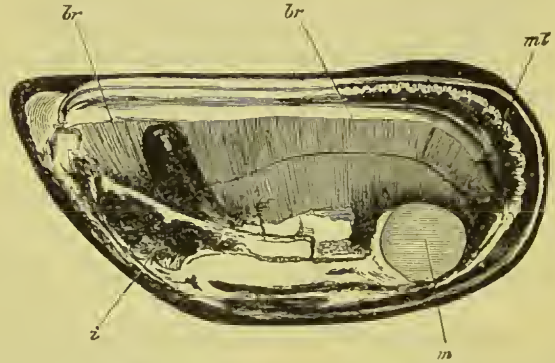

Fig. 82.—VALVE OF MUSSEL (MYTILUS EDULIS) SHOWING *br*, *br*, THE EXPANDED GILLS OR BRANCHIÆ, WHICH, OWING TO THE LITTLE BARS OF WHICH THEY ARE COMPOSED, PRESENT A STRIATED ASPECT.

ml, mantle; *m*, cut adductor muscle; *i*, mass of viscera; the dark projection just above is the foot.

Keep this preparation until the end of the lesson, by which time many of the cilia will have become languid. When this is the case pass a drop of dilute potash solution (1 part KHO to 1000 of sea-water) under the cover-glass and observe the effect.

4. Cement with sealing-wax a piece of small glass tubing to a slide so that one end of the tube comes nearly to the centre of the slide. To do this effectually the slide must be heated and some sealing-wax melted on to it and allowed to cool. The glass tube is then made hot and applied to the

slide, embedding itself as it does so in the sealing-wax. Apply a ring of modelling wax (half an inch in diameter and rising above the glass tube) so as to include the end of the tube. Make a deep notch or a hole in the ring opposite the tube for the exit of the gas. Place a drop of water within the ring (fig. 83).

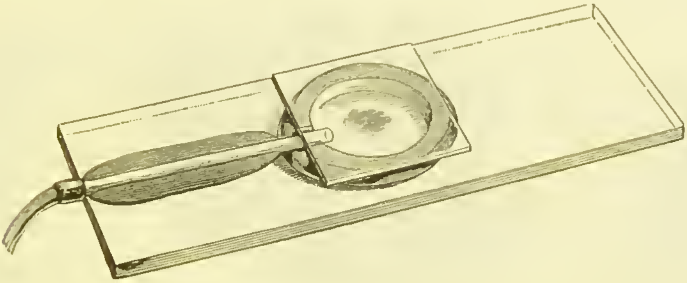

Fig. 83.—Moist chamber adapted for passing a gas or vapour to a preparation under the microscope.

Put a bar from the gill upon a cover-glass in the least possible quantity of sea-water; invert the cover-glass over the putty ring, and press it gently and evenly down. The preparation hangs in a *moist chamber* within which it can be studied through the cover-glass, and into which gases or vapours can be passed and their effects observed.

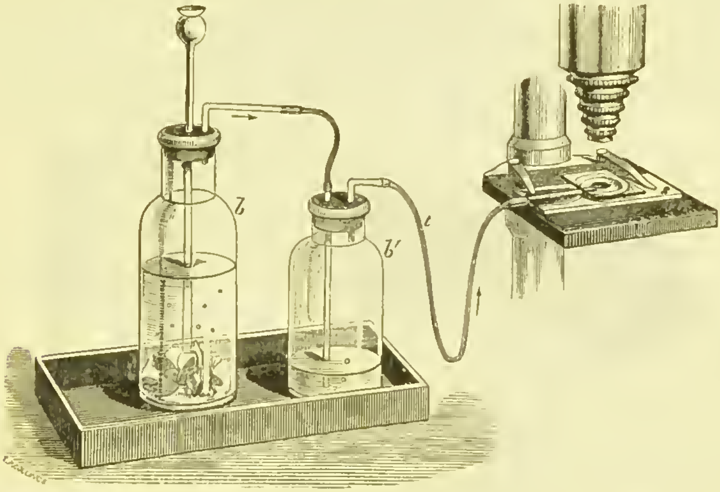

Fig. 84.—Method of subjecting a preparation to a stream of carbon dioxide.

b, bottle containing marble and hydrochloric acid; *b′*, wash-bottle, connected by india-rubber tube, *t*, with the moist chamber, *s*.

Pass CO_2 through the chamber, and after observing the effect replace it by air (see fig. 84). Repeat with ether vapour and with chloroform vapour.

Columnar epithelium and **ciliated epithelium** are for the most part found covering the inner surface of mucous membranes; which are membranes moistened by *mucus* and lining passages in communication with the exterior, such as the alimentary canal and the respiratory and generative passages. The cells of a columnar epithelium form a single layer, varying in thickness according to the length of the constituent cells, and when the cells of a columnar epithelium are short, the epithelium is spoken of as cubical, such as that which lines the vesicles of the thyroid gland (fig. 85). The cells of a columnar epithelium (fig. 86) are prismatic columns, which are set closely side by side, so that when seen from the surface a mosaic appearance is produced. They often taper somewhat towards their attached end, which is generally truncated, and set upon a basement membrane. Their free surface is covered by a thick striated border (figs. 86 to 89) which may sometimes become detached in teased preparations. The

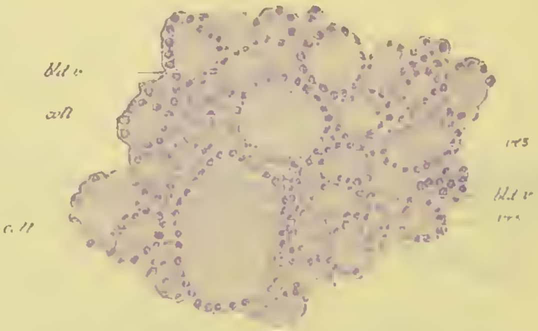

Fig. 85.—Section of thyroid of cat, showing gland-vesicles lined with cubical epithelium. (Vincent and Jolly.)

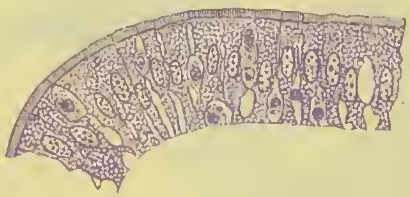

Fig. 86.

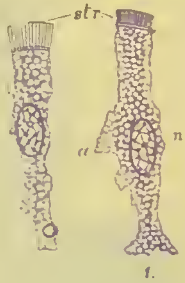

Fig. 87.

Fig. 86.—A row of columnar cells from the intestine of the rabbit. Smaller cells are seen between the epithelium-cells; these are leucocytes.

Fig. 87.—Columnar epithelium-cells of the rabbit's intestine. More highly magnified.

The cells have been isolated after maceration in very weak chromic acid. The cells are much vacuolated, and one of them has a fat-globule adhering to it near its attached end; the striated border (*str*) is well seen, and the bright disk separating it from the cell-protoplasm; *n*, nucleus, with intranuclear network; *a*, a thinned-out wing-like projection of the cell which probably fitted between two adjacent cells.

protoplasm of the cell is highly vacuolated and reticular, and fine longitudinal striæ may be seen in it (figs. 88, 89). Between the striated border and the protoplasm of the cell is a highly refracting

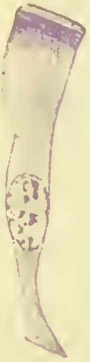

FIG. 88.

FIG. 88.—A COLUMNAR EPITHELIUM-CELL, SHOWING MASS OF FIBRILS (CYTOMITOME) WITHIN THE CYTOPLASM. (M. Heidenhain.)

FIG. 89.—A GOBLET OR MUCUS-SECRETING CELL IN COLUMNAR EPITHELIUM. (M. Heidenhain.)

The centrosome is in the mucigen-mass. Part of an ordinary columnar cell is also shown.

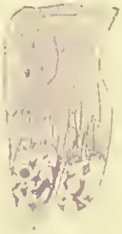

FIG. 89.

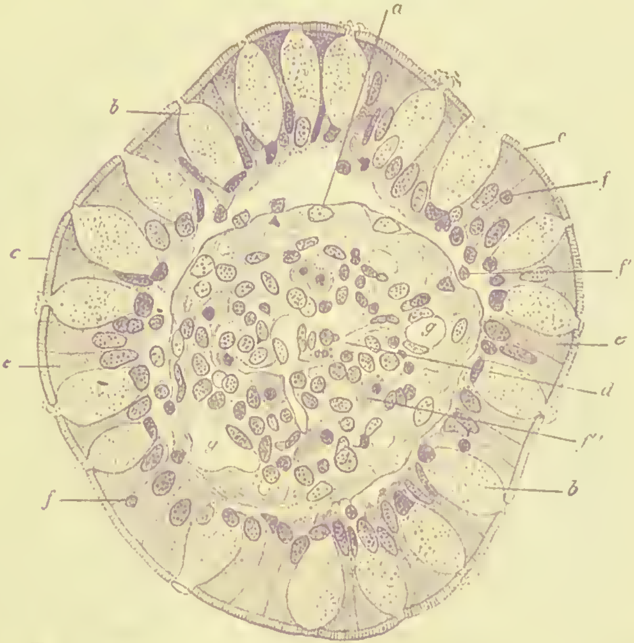

FIG. 90.—TRANSVERSE SECTION OF A VILLUS (MAN), SHOWING NUMEROUS GOBLET-CELLS BETWEEN THE ORDINARY COLUMNAR CELLS. (v. Ebner.) Magnified 530 diameters.

a, basement-membrane, here somewhat shrunken away from epithelium; *b*, goblet-cells; *c*, cuticula; *d*, lacteal; *e*, columnar epithelium; *f*, leucocytes in epithelium; *f'*, leucocytes below epithelium; *f''*, large leucocytes; *g*, blood-vessels.

disk which contains fine dumb-bell shaped particles set vertically, connected below with the fibrils or striæ which run through the cell protoplasm. It has been suggested that these particles are formed by multiplication of the centrosome, but the fact cannot be regarded as established. The nucleus is ovoid and reticular. The lateral borders of the cells are often somewhat irregular or jagged, the result of the presence of amœboid cells, which are generally found between the columnar cells, at least in the intestine. After a meal containing fat the epithelium-cells of the small intestine contain fat globules, which become stained black in osmic preparations.

Columnar epithelium-cells are found lining the whole of the interior of the stomach and intestines: they are also present in the ducts of most glands, and sometimes also in their secreting tubes and saccules. The epithelium which covers the ovary is also of a modified columnar shape, but cells having *all* the structural peculiarities indicated above are found only in the alimentary canal and in its diverticula.

Goblet-cells.—Some of the cells of most columnar epithelia (fig. 90), and also cells of glandular, ciliated, and transitional epithelia, contain mucigen, which is laid down within the cell in the form of granules (fig. 89, fig. 91, m^1, m^2). These granules eventually swell up to form globular masses which may run together and greatly distend the part of the cell nearest the free border. When the mucigen is extruded as mucus the cell takes the form of a goblet or chalice, hence the name.

These *goblet-cells*, or as they are more appropriately termed, *mucus-secreting cells*, are probably not mere temporary modifications of the ordinary columnar and ciliated cells amongst which they are found, but permanently differentiated cells, which, after having got rid of their mucus by extrusion, again form a fresh supply in the same way as before. In the gastric mucous membrane all the surface epithelium is composed of mucus-secreting cells, and they extend also into the mouths of the glands. In the large intestine also most of the cells both of the surface and in the glands are goblet-cells. According to the observations of Carlier those of the gastric mucous membrane are connected together laterally by protoplasmic fibres.

Ciliated epithelium.—Ciliated epithelium is found in man throughout the whole extent of the air-passages and their prolongations, but not in the uppermost part of the nostrils which is supplied by the olfactory nerves, nor in the lower part of the pharnyx, nor in the terminal bronchioles and pulmonary alveoli. It also occurs in the Fallopian tubes and the greater part of the uterus; in the efferent tubes of the testicle; and in the ventricles of the brain, and the central canal of the spinal cord. The cells of a ciliated epithelium are usually columnar in shape (figs. 91, 92), but in place of the striated border of the ordinary columnar cell the free surface is surmounted by a bunch of fine tapering

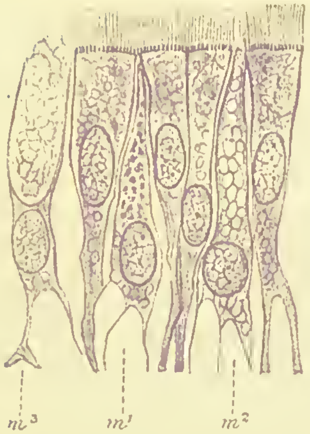

FIG. 91.—CILIATED COLUMNAR EPITHELIUM, FROM THE TRACHEA OF A RABBIT.

m^1, m^2, m^3, mucus-secreting cells in various stages of mucigen formation. The preparation was treated with dilute chromic acid.

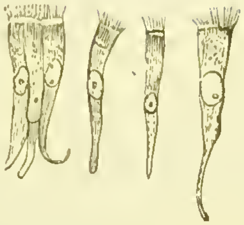

FIG. 93.—COLUMNAR CILIATED EPITHELIUM-CELLS FROM THE LOWER PART OF THE HUMAN NASAL PASSAGES. EXAMINED FRESH IN SERUM.[3] (Sharpey.)

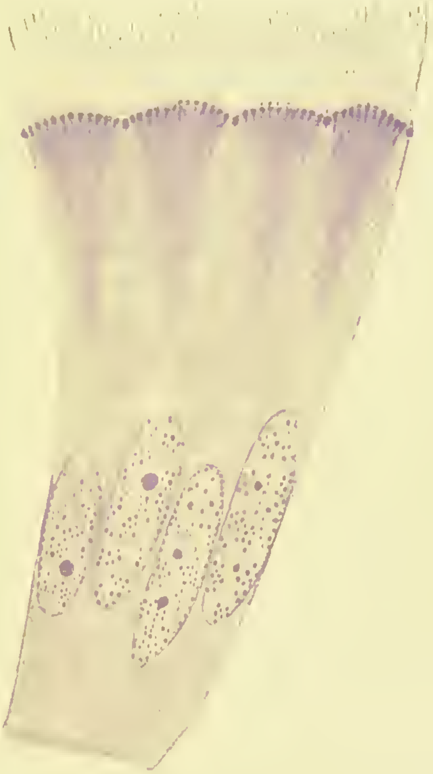

FIG. 92.—FOUR CILIATED CELLS. (v. Lenhossék.)

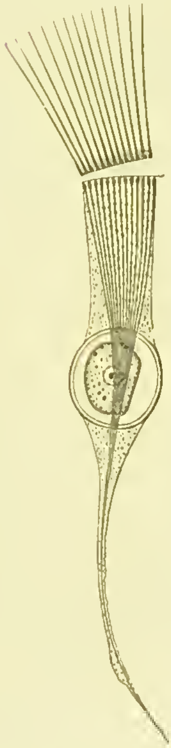

FIG. 94.—CILIATED CELL, FROM THE INTESTINE OF A MOLLUSC. (Engelmann.)

filaments (*vibratile cilia*), which, during life, move spontaneously to and fro, and serve to produce a current in the fluid which covers them. The border upon which the cilia are set is bright in the living condition: after fixation it appears formed of little juxtaposed *knobs* or *basal particles*, to each of which a cilium is attached.

In the large ciliated cells which line the alimentary canal of some molluscs (figs. 92, 94), and with less distinctness in the ciliated cells of vertebrates, the knob may be observed to be prolonged into the protoplasm of the cell as a fine varicose filament, termed the *rootlet* of the cilium. Since the axial fibril in the tail of the spermatozoon (which is commonly regarded as a cilium) is developed in connection with the centrosome, it has been supposed that the cilia of an ordinary ciliated cell may also be outgrowths from the (multiplied) centrosome. But although it may be the case that the basal particles are formed by the division of the centrosome of the cell, in which case the rootlets may represent the fibrils of archoplasm which radiate from the centrosome of such a cell as the white corpuscle (fig. 11), it appears not to be true that the cilia are developed from these basal particles, for the cilia sometimes appear before the basal particles. In plant spores, which have no centrosomes, the cilia are developed from amœboid processes of the ectoplasm of the cell (Strassburger). Similar basal particles and longitudinal fibrils are found in columnar cells (p. 75), and these are probably homologous with the knobs and rootlets of the ciliated cell, while the bunch of cilia of the latter is represented by the striated border of the columnar cell.

The action of cilia.—When in motion a cilium is bent quickly over in one direction with a lashing whip-like movement, immediately recovering itself. When vigorous the action is so rapid, and the rhythm so frequent (ten or more times in a second), that it is impossible to follow the motion with the eye. All the cilia upon a ciliated surface are not in action at the same instant, but the movement travels in waves over the surface. If a cell is detached from the general surface, its cilia continue to act for a while, but their movement at once ceases if they are detached from the cell. If, however, a portion of the cell protoplasm is detached with them, they will continue to move for a time.

The rhythm is slowed by cold, quickened by warmth; but heat beyond a certain point kills the cells. The movement will continue for some time in water deprived of oxygen. Both CO_2 gas and ether and chloroform vapour arrest the action, but it recommences on restoring air, if their action is not too prolonged. Dilute alkaline solutions quicken the activity of cilia, or may even restore it shortly after it has ceased.

Theories of ciliary action.—Various attempts have been made to explain the manner in which cilia act. One hypothesis supposes that one side only of each cilium is contractile, the other side being elastic, or that there is a more rigid but elastic axis and a contractile covering. It is, however, impossible that a soft structure like a cilium could be bent over in a uniform curve by contraction along one side; such contraction could only produce shortening and wrinkling of the cilium, effects which are never observed. Another hypothesis assumes that the projecting cilia are set in action by rhythmic lateral contractions in the protoplasm; which, by moving the rootlets, cause the cilia to bend over as a whip is bent by movements of the wrist applied to its handle. But this again implies an amount of rigidity which neither the cilia nor the rootlets possess, for it must be borne in mind that they have to overcome the resistance of fluid, and of fluid which is in many cases highly viscous.

The simplest hypothesis appears to be that they are curved flattened hollow filaments, the interior communicating with the cell-protoplasm. All cilia and cilium-like structures (flagella) which are sufficiently large to show any structural differentiation, exhibit an external membranous covering and a clear and usually structureless contents, but the minute size of ordinary cilia prevents one from determining whether this is also the case with them. If it is the case, then rhythmical variations of pressure within the cell-protoplasm, which might, as in the case of amoeboid movements, be caused by alterations in surface tension, would be transmitted to the cilia and would cause the curve to open out, and again to assert itself, according to the degree of tension within the tubular filament. Such action can be imitated with a curved flattened flexible tube attached to a pressure bag (fig. 95). Any increase of pressure causes the tube to straighten out; on again decreasing the pressure the tube bends over exactly in the manner of a cilium. This hypothesis has the advantage over the others which have been offered that it explains the movements of cilia on a theory which is similar to that which gives the most probable explanation of amoeboid movements of protoplasm, viz., that they are due to variations in surface tension, and it thus brings these two forms of protoplasmic activity into line with one another. It will presently be shown that the changes which occur in muscle in contraction are susceptible of a similar explanation.

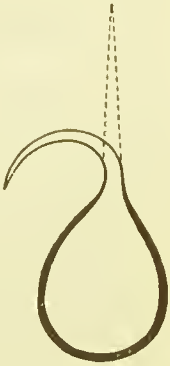
FIG. 95.—MODEL TO ILLUSTRATE THE ACTION OF A CILIUM.

LESSON IX.

THE CONNECTIVE TISSUES.

AREOLAR AND ADIPOSE TISSUE. RETIFORM TISSUE.

1. TAKE a little of the subcutaneous tissue or of the intermuscular connective tissue of a rabbit or guinea-pig and spread it out with needles on a dry slide into a large thin film. Keep the centre moist by occasionally breathing on it, but allow the edges to dry to the slide. Before commencing put a drop of salt solution on a cover-glass, and now invert this over the film. Examine with a high power. Sketch one or two bundles of white fibres and also one or two elastic fibres, distinguishable from the former by their sharp outline, isolated course, and by their branching. Sketch also one or more connective-tissue corpuscles, if any such are visible in the clear interspaces. Look also for migratory cells (leucocytes). Next carefully remove the cover-glass and replace the salt solution by dilute acetic acid (1 per cent.). Watch its effect in swelling the white fibres and bringing more clearly into view the elastic fibres and corpuscles. Look for constricted bundles of white fibres.

2. Make another very thin film in the same way, but allow to dry completely. Pour over the film a 1 per cent. solution of magenta in 50 per cent. alcohol, to which 1 drop per cubic centimeter of a 1 per cent. solution of gentian violet in alcohol has just been added. After one minute drain this off, wipe round the specimen and allow the remainder of the staining solution to dry on the film. When completely dry mount in dammar. The elastic fibres are deeply stained; the cells are also well shown.[1]

3. Prepare another film of the subcutaneous tissue, including a little adipose tissue. Fix by pouring over it formol (10 p.c.) and leave this in contact with the film for 20 minutes. Wash with water and stain with saturated solution of Sudan III. or Scharlach R. in 75 p.c. alcohol; wash with 75 p.c. alcohol to remove stain from everything except fat, then wash with water and stain with dilute hæmatoxylin. Mount in glycerine and water. Examine first with a low and afterwards with a high power. The fat is well brought out by the Sudan III. or Scharlach R. stain: if the preparation is from a young animal, fat-cells will be found in process of formation. Measure and sketch two or three of the cells.

The fat may also be stained, without prior fixation, by treatment with 1 p.c. osmic acid solution.

4. Spread out another large film of connective tissue, letting its edges dry to the slide, but keeping the centre moist by the breath. Place on its centre a large drop of nitrate of silver solution (1 per cent.). After five minutes wash this away with distilled water, and expose to direct sunlight until slightly brown. Now allow the film to dry completely, and cover it in dammar varnish or Canada balsam dissolved in xylol. Sketch the outlines of two or three of the cell-spaces.

5. To display retiform tissue the following method is recommended by Spalteholz. Place a piece of the organ (*e.g.* lymphatic gland) for twenty-

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[1] Mallory's stain (see Appendix) may also be used for connective-tissue fibres.

four hours or more in alcohol, then overnight at 38° C. in a 1 per cent. solution of carbonate of soda to which a few drops of a solution containing trypsin have been added. Cautiously transfer the semi-digested structure to alcohol again, and leave it for a few hours. Embed in paraffin in the usual way and stain the sections with iron hæmatoxylin. The fibrils of connective and retiform tissue are the only structures which have remained undigested and they are deeply coloured by the hæmatoxylin.

The **connective tissues** include *areolar* tissue, *adipose* tissue, *elastic* tissue, *fibrous* tissue, *reticular* and *lymphoid* tissue, *cartilage* and *bone.* All these tissues agree in certain microscopical and chemical characters. They, for the most part, have a large amount of intercellular substance in which fibres are developed, and these fibres are of two kinds—*white* and *yellow* or *elastic.* Moreover, there are many points of similarity between the cells which occur in these tissues; they are all developed from the same embryonic formation, and they tend to pass imperceptibly the one into the other. Besides this, the use of these several tissues is similar; they mostly serve to connect and support the other tissues, performing thus a passive mechanical function. They may therefore be grouped together, although differing considerably in external and even in microscopic characters. Of the connective tissues, however, there are three which are so intimately allied as to be naturally considered together, being composed of exactly the same elements, although differing in the relative development of those

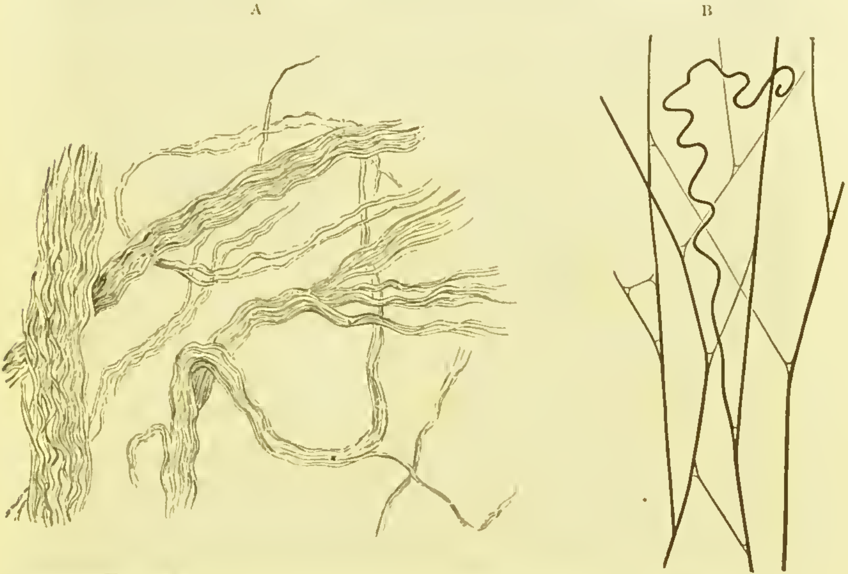

FIG. 96.—WHITE AND ELASTIC FIBRES OF AREOLAR TISSUE.
A, bundles of white fibres partly unravelled. B, elastic fibres.

elements: these are the areolar, elastic, and fibrous tissues. Adipose tissue and reticular tissue may both be looked upon as special modifications of areolar tissue. Areolar tissue being the commonest and, in a sense, the most typical, its structure may be considered first.

Areolar tissue.—The areolar tissue presents to the naked eye an appearance of fine transparent threads and laminæ which intercross in every direction with one another, leaving intercommunicating meshes, or areolæ, between them. When examined with the microscope, these threads and fibres are seen to be principally made up of wavy bundles of exquisitely fine transparent fibres (*white fibres*, fig. 96, A). The bundles run in different directions, and may branch and intercommunicate with one another (fig. 99); but the individual fibres, although they pass from one bundle to another, never branch or join other fibres. The fibres are cemented together into the bundles by a clear substance containing mucin, and the same clear material forms also the basis or *ground-substance* of the tissue, in which the bundles themselves course, and in which also the corpuscles of the tissue lie embedded. This ground-substance between the bundles can with difficulty be seen in the fresh tissue on account of its extreme transparency; but it can be brought to

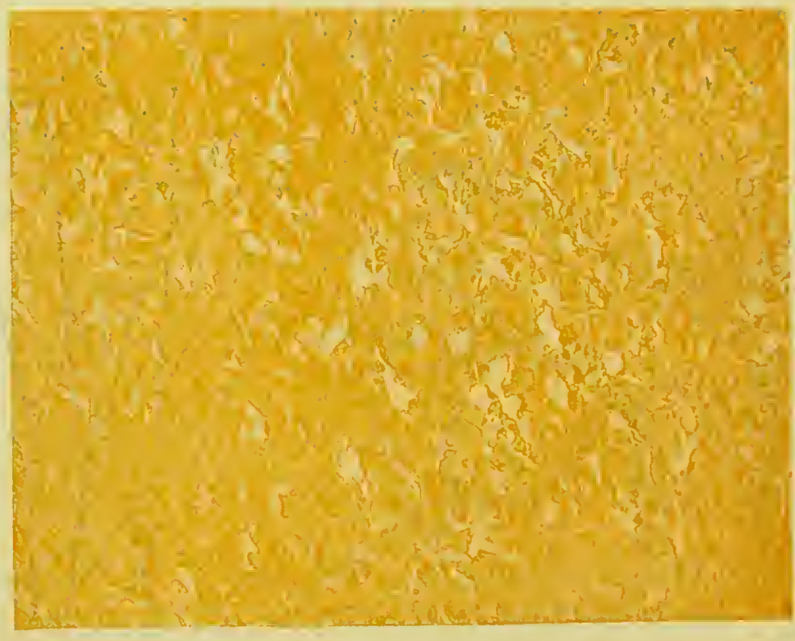

FIG. 97.—AREOLAR TISSUE PREPARED BY RECKLINGHAUSEN'S SILVER METHOD. Magnified 200 diameters. Photograph.

The cells are seen as clear spaces in the (brown) stained ground-substance, through which the fibres course.

view by staining with nitrate of silver, as in § 4. The whole of the tissue is thereby stained of a yellowish brown colour, with the exception of the spaces which are occupied by the corpuscles (*cell-spaces*, fig. 97). As Macallum has shown, this reaction is due to the presence of chlorides in the intercellular substance, whereas the cell-protoplasm contains none.

Besides the white fibres of connective tissue here described, fibres of a different kind (fig. 96, B) may be made out in the preparations; these are the *elastic fibres*. They are especially well seen after treatment with acetic acid, and after staining with magenta, or, in sections, with orcein; but they can be detected also in the fresh preparation, They are characterised by their distinct outline, their straight course, the fact that they never run in bundles, but singly, and that they branch or join neighbouring fibres. If broken by the needles in making the preparation, the elastic recoil causes them to curl up, especially near the broken ends. Besides these histological differences, the two kinds of fibres differ also in their chemical characters. Thus the white fibres are formed of a material (*collagen*) which is dissolved by boiling in water yielding gelatin, and by peptic digestion, but is not dissolved by tryptic digestion; whereas the substance of which the elastic fibres are composed (*elastin*) resists for a long time the action of boiling water and peptic digestion, although it is dissolved by tryptic digestion. Moreover, the white fibres swell and become indistinct under the action of acetic acid; the elastic fibres are unaltered by this reagent. Elastic fibres appear to have a sheath which is more resistant to reagents than the rest of the fibre.

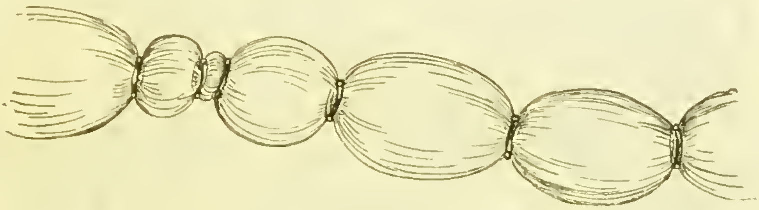

FIG. 98.—A WHITE BUNDLE SWOLLEN BY ACETIC ACID. FROM THE SUBARACHNOID TISSUE AT THE BASE OF THE BRAIN. (Toldt.)

The bundles of white fibres which have been swollen out by acid sometimes exhibit constrictions at irregular intervals (fig. 98). These are in many instances due to elastic fibres coiling round the white bundles.

The cells of areolar tissue.—Several varieties of connective-tissue cells are distinguished, viz.: (1) *Lamellar cells*, which are flattened and often branched (figs. 99, 100, *c*, *c'*), and may be united one to the other by their branches, as in the cornea (fig. 101). Sometimes they are unbranched and may lie along the fibril-bundles and even themselves show a fibrillar appearance (fig. 99, *f*). Some authors have inferred from this that these cells are transformed into white fibril-bundles and have termed them "fibroplasts"; but the fibrillation which they exhibit is not of the same character as that of the white fibres, and is probably a form of cytomitome, such as is seen in many protoplasmic cells. In certain situations the lamellar connective-tissue cells are greatly flattened out, especially when they lie upon the surface of aponeuroses and they are there joined edge to edge like the cells of an endothelium (fig. 103. The apparent cell-spaces in silver preparations have of course in all cases a similar arrangement to that of the cells). (2) *Clasmatocytes*, which are composed of a soft, much-vacuolated, often granular protoplasm, rarely flattened, but otherwise varying greatly in shape and size (fig. 99, *p*; fig. 100, *d*). (3) *Mast-cells* (*Mast-zellen* of Ehrlich), usually spheroidal or ovoidal in shape, and formed, like the plasma-cells, of soft protoplasm, but thickly occupied with granules, which are deeply stained by gentian violet and by other basic aniline dyes. They are

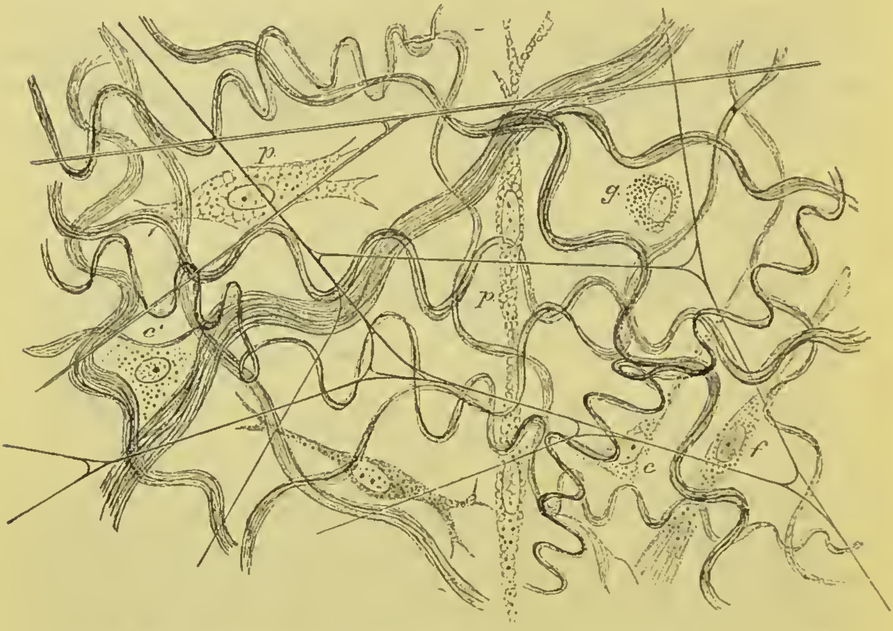

FIG. 99.—SUBCUTANEOUS TISSUE FROM A YOUNG RABBIT, PREPARED AS DIRECTED IN § 1. Highly magnified.

The white fibres are in wavy bundles; the elastic fibres form an open network. *p*, *p*, clasmatocytes; *g*, plasma-cell; *c*, *c'*, lamellar cells; *f*, fibrillated cell.

not everywhere common, but are numerous in parts where fat is being laid down (fig. 106). (4) *Plasma-cells.* These are characterised by their granular protoplasm, which is less basiphil than that of the mast-cells; their small spheroidal nucleus; and their shape, which is usually rounded or only slightly branched.

Migratory leucocytes may also (fig. 100, *e*) be seen here and there in the areolar tissue (*wander-cells*).

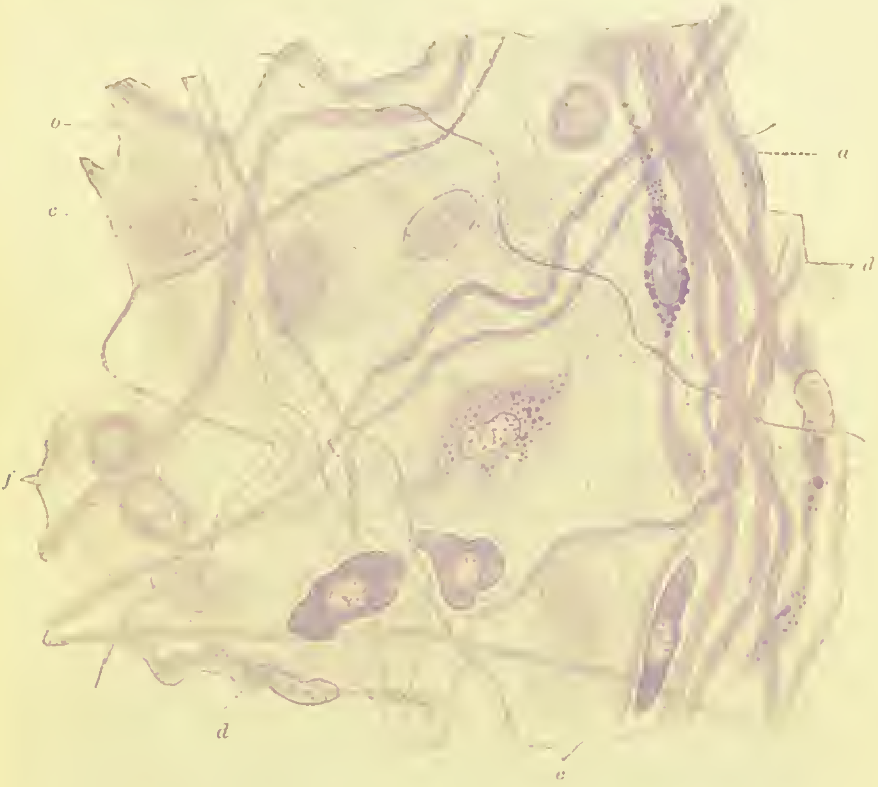

Fig. 100.—Fibres and cells of areolar tissue of a guinea-pig from a film preparation. (Maximow.) The preparation was stained, without fixation, by neutral red.

a, bundles of white fibres; *b*, elastic fibres; *c*, lamellar cells; *d*, clasmatocytes; *e*, plasma-cells; *f*, oxyphil leucocytes.

In the middle coat of the eye in mammals, and in some parts of the skin, some of the connective-tissue cells are occupied by granules of pigment (*pigment-cells*).

These are much more extensively present in lower vertebrates, especially in amphibia and fishes, where they exhibit amœboid changes which result in the pigment being at one time diffused over a considerable area and at another time restricted to the immediate neighbourhood of the nucleus.

The changes thus produced cause alteration in the general colour and shade of the integument, where such pigment cells are very numerous, and serve the purpose of protective adaptation of the animals to their environment.

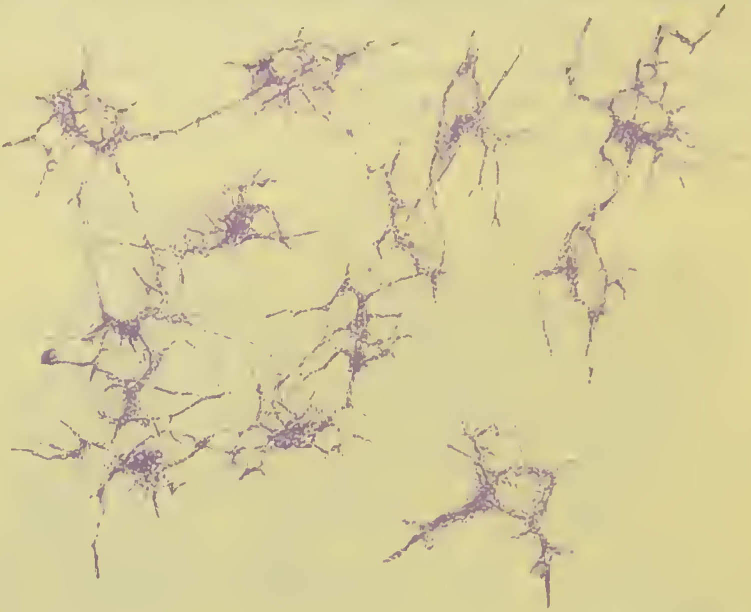

FIG. 101.—CELLS OF RABBIT'S CORNEA STAINED WITH GOLD CHLORIDE. Magnified 300 diameters.

The nuclei are unstained. The cells are connected by their branches.

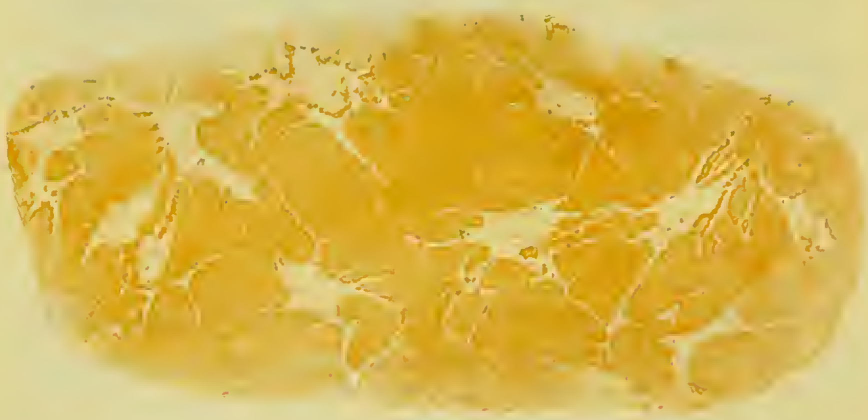

FIG. 102.—CORNEA OF RABBIT, STAINED WITH SILVER NITRATE. Magnified 300 diameters. Photographed from a preparation by H. Pringle.

The cells are unstained, and appear as white spaces on a brown ground. Compare with fig. 101, in which the corneal cells are stained.

The connective-tissue cells occupy spaces of corresponding shape in the ground-substance (fig. 102), between the bundles of white fibres. In some parts of the connective tissue the white bundles are developed

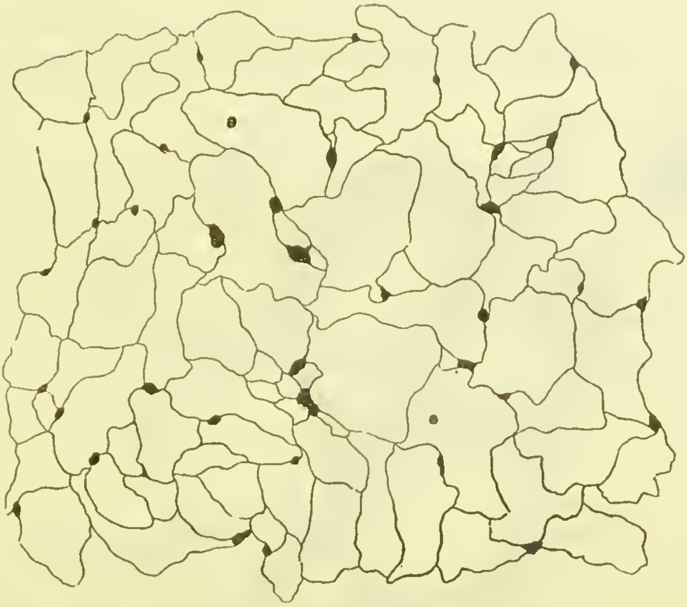

FIG. 103.—EPITHELOID CELLS OF CONNECTIVE TISSUE FROM THE SURFACE OF AN APONEUROSIS. (Nitrate of silver preparation.)

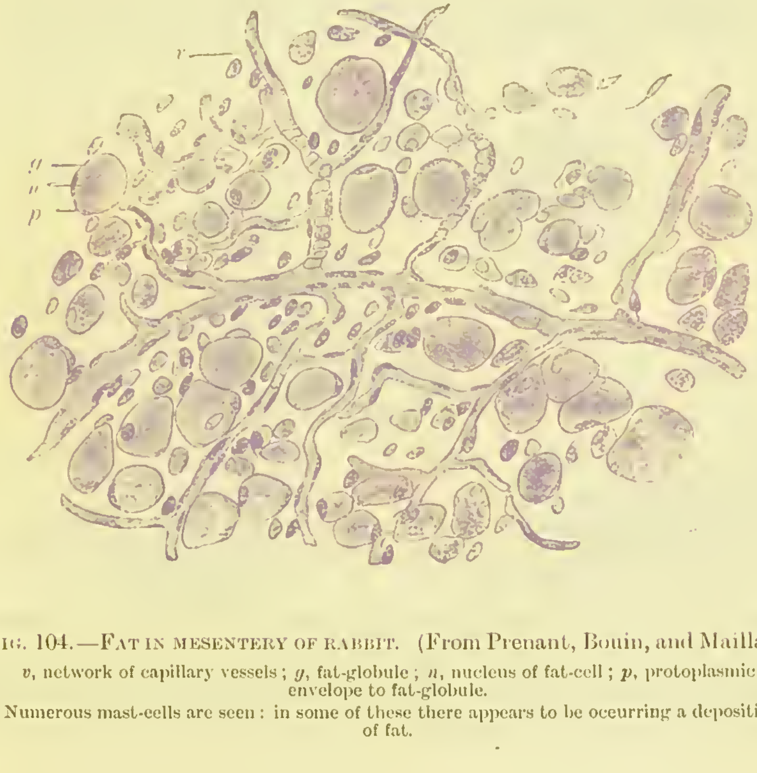

FIG. 104.—FAT IN MESENTERY OF RABBIT. (From Prenant, Bouin, and Maillard.)

v, network of capillary vessels; *g*, fat-globule; *n*, nucleus of fat-cell; *p*, protoplasmic envelope to fat-globule.

Numerous mast-cells are seen: in some of these there appears to be occurring a deposition of fat.

to such an extent as to pervade almost the whole of the ground-substance, and then the connective-tissue corpuscles become squeezed into the interstices, flattened lamellar expansions of the cells extending between the bundles, as in tendon (see next Lesson).

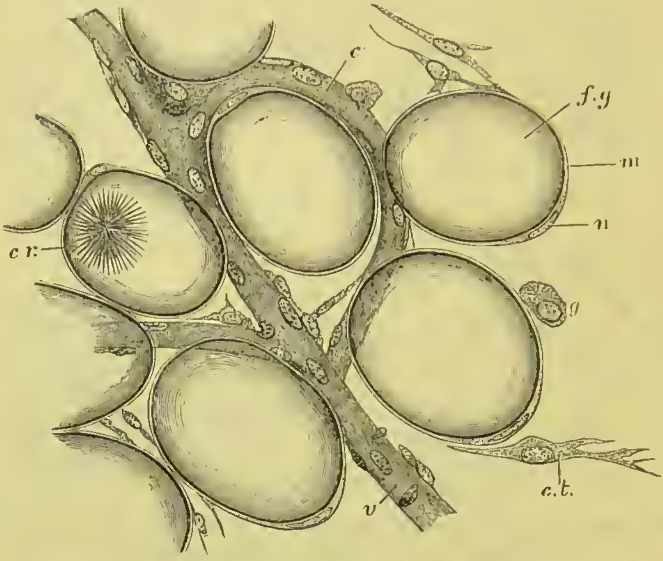

FIG. 105.—A FEW CELLS FROM THE MARGIN OF A FAT LOBULE. Highly magnified.

f.g., fat-globule distending a fat-cell; *n*, nucleus; *m*, membranous envelope of the fat-cell; *c.r.*, bunch of crystals within a fat-cell; *c*, capillary vessel; *v*, venule; *c.t.*, connective-tissue cell; *g*, granular cell. The connective-tissue fibres are not represented.

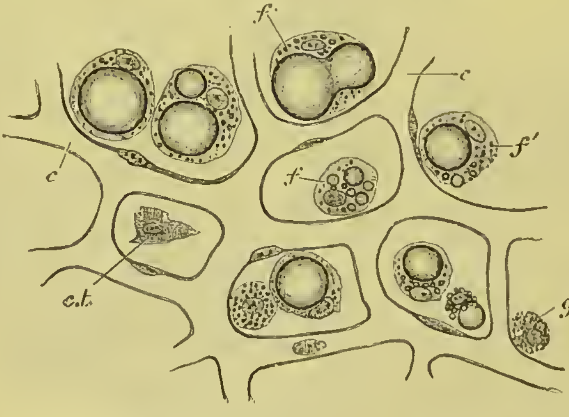

FIG. 106.—DEPOSITION OF FAT IN CONNECTIVE-TISSUE CELLS.

f, a cell with a few isolated fat-droplets in its protoplasm; *f'*, a cell with a single large and several minute drops; *f''*, fusion of two large drops; *g*, granular mast-cell; *c.t.*, lamellar connective-tissue corpuscle; *c*, *c*, network of capillaries.

The cells and cell-spaces of areolar tissue come into intimate relation with the cells lining the lymphatic vessels and small blood-vessels.

This connection can best be seen in silvered preparations; it will be again referred to in speaking of the origin of the lymphatics.

Adipose tissue consists of vesicles filled with fat (figs. 104, 105, 107) and collected into lobules, or into tracts which accompany the small blood-vessels. The vesicles are round or oval in shape, except where closely packed, when they become polyhedral from mutual compression. The fat-drop is contained within a delicate protoplasmic envelope (fig. 105, *m*) which is thickened at one part, and here includes an oval flattened nucleus. The fat is stained black by osmic acid; a deep yellow colour by Sudan III.; and an intense red by Scharlach R. The vesicles are supported partly by filaments of areolar tissue, but chiefly by a fine network of capillary blood-vessels.

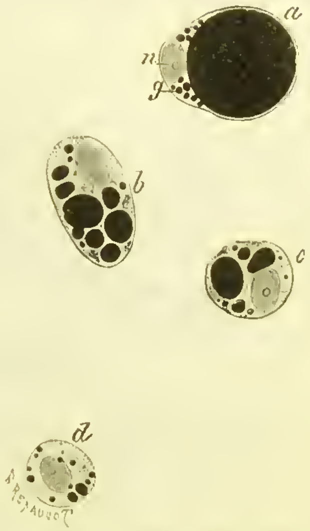

Fig. 107.—Fat-cells from young animal. (Ranvier.) Osmic acid preparation.

The drops of fat are stained of an intense black. *n*, nucleus; *g*, small globules of fat.

The fat when first formed in the embryo is in some situations deposited within large granular cells (fig. 108) of a spheroidal or polyhedral shape; some authorities regard these cells as of a specific nature, for they are in certain situations collected into large gland-like masses (fig. 108) abundantly supplied with blood-vessels, and gradually become transformed into fat-cells by the deposition of fat in the

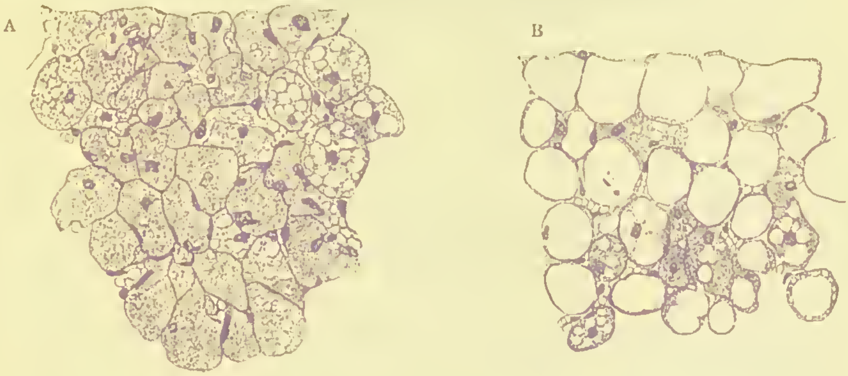

Fig. 108.—Two stages of formation of adipose tissue. (H. Batty Shaw.)

In A the tissue is formed of a gland-like mass of cells, in some of which the cytoplasm is occupied by fat globules (looking white in the sections). In B the fat fills many of the cells.

cell-protoplasm. Fat is, however, also laid down in other situations in the ordinary more loosely arranged flattened or branched cells of connective tissue. The fat appears to be produced by a transformation into droplets of fat of albuminous granules which the cells produce. As the droplets increase in size they run together into a larger drop, which gradually fills the cell more and more, swelling it out so that the cell-protoplasm eventually appears merely as the envelope of the fat vesicle.

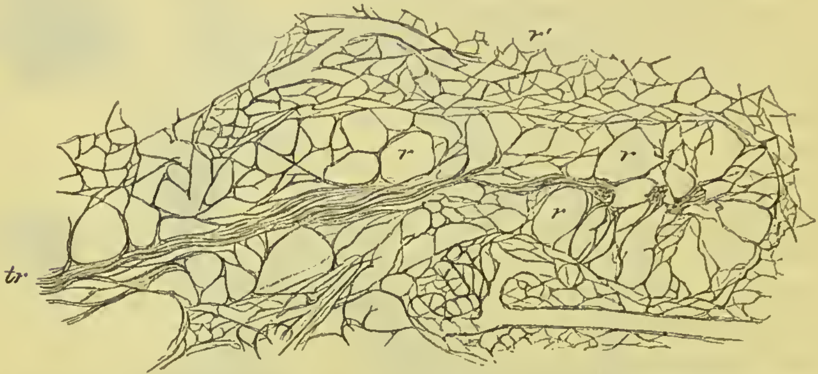

Fig. 109.—Retiform tissue from a lymph-gland. Moderately magnified.

tr, a trabeculum of connective tissue; *r*, *r'*, retiform tissue, with more open meshes at *r* and denser at *r'*.

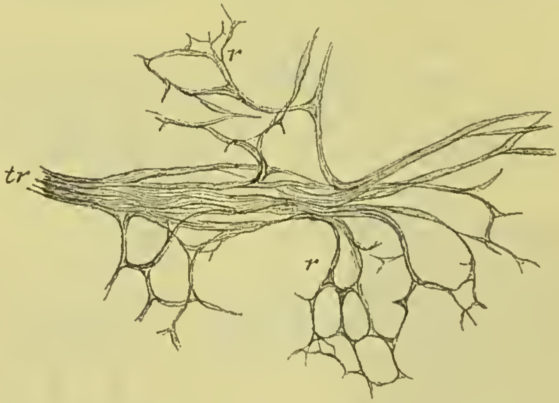

Fig. 110.—Portion of the above, more highly magnified.

showing the continuity of the retiform tissue, *r*, *r*, with the connective tissue of a trabeculum, *tr*.

Fat is found most abundantly in subcutaneous areolar tissue, and under the serous membranes; especially in some parts, as at the back of the peritoneum around the kidneys, under the epicardium, and in the mesentery and omentum. The yellow marrow of the bones is also principally composed of fat. There is no adipose tissue within the cavity of the cranium.

RETICULAR AND LYMPHOID TISSUE.

Retiform or reticular tissue (figs. 109, 110, 111) is a variety of connective tissue in which the intercellular or ground substance has largely disappeared or is replaced by fluid. There are very few or no elastic fibres in it, but a dense network of white fibres, the meshes of which vary in size, being very small and close in some parts; more open and like areolar tissue in other parts. In some places where the tissue occurs the fibres are enwrapped by flattened branched connective-tissue cells, and until these are removed it is not easy to see the fibres. Chemical differences between the fibres of retiform tissue and those of ordinary areolar tissue have been described, but microscopically the fibres of the two tissues are indistinguishable and are found in continuity with one another (see figs. 110, 112). This tissue forms a fine framework in many organs, supporting the proper elements and extending into all the interstices between the coarser connective-tissue bundles. It can be well shown by dissolving the cells of the tissue by tryptic digestion and subsequently staining the fibres forming the reticulum (p. 80, § 5). In this way it may be demonstrated in lymph-glands, in the spleen, liver, bone-marrow (fig. 111), mucous membranes, and many other parts.

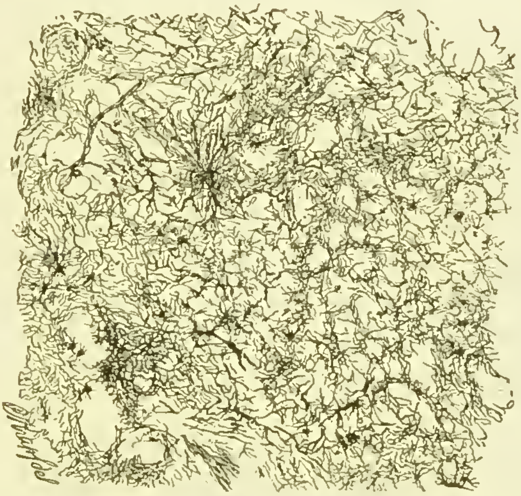
FIG. 111.—RETICULUM OF BONE-MARROW. (Enderlen.)

Lymphoid or **adenoid tissue** is reticular tissue in which the meshes of the network are largely occupied by lymph-corpuscles (fig. 112). This is by far the most common condition of a retiform tissue, and is met with in the lymph-glands and allied structures, in parts of the alimentary mucous membrane, and in various other situations.

Basement-membranes *(membranæ propriæ)* are homogenous-looking membranes, which are found forming the surface layers of connective tissue expansions in many parts, especially where there is a covering of epithelium, as on mucous membranes, in secreting glands, and elsewhere. They are generally formed of flattened connective-tissue cells joined together to form a membrane; but in some cases they are evidently formed not of cells, but of condensed ground-substance, and in yet other cases they are composed of elastic substance; the name basement-membrane has therefore been used to denote structures of an entirely different nature.

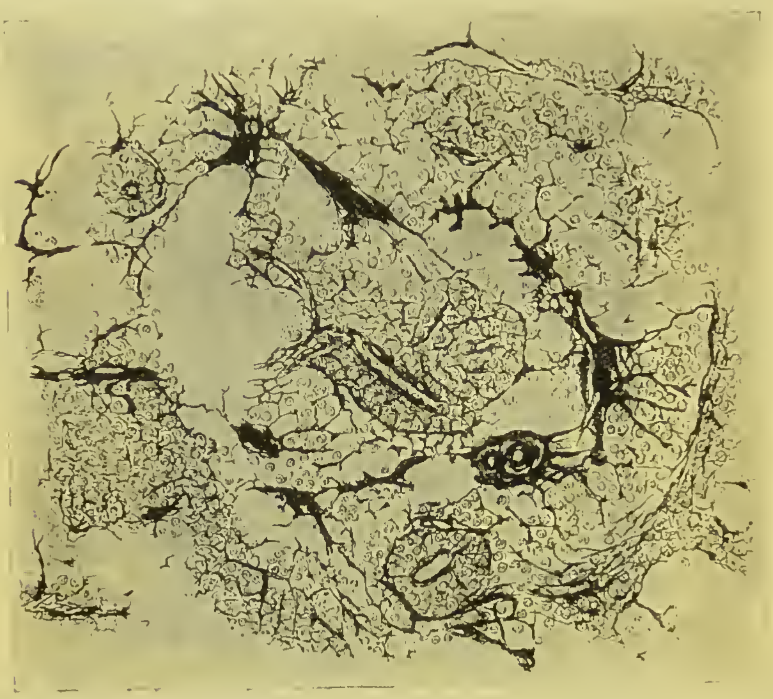

Fig. 112.—Lymphoid tissue of a lymph-gland.

Jelly-like connective tissue, although occurring largely in the embryo, is found only in one situation in the adult—viz. forming the vitreous humour of the eye. It is composed mainly of soft, fluid, or semi-fluid ground-substance, with cells scattered here and there through it, and with a few fibres which interlace throughout the tissue and confine the fluid of the ground-substance within their meshes; thus conferring upon the tissue its jelly-like character. All embryonic connective tissue is at one period of this jelly-like nature (see p. 101).

LESSON X.

THE CONNECTIVE TISSUES (continued).

ELASTIC TISSUE. FIBROUS TISSUE. DEVELOPMENT OF CONNECTIVE TISSUE.

1. TEASE out as finely as possible a small shred of elastic tissue (ligamentum nuchæ of the ox or ligamentum subflavum of man) in glycerine and water, slightly coloured by magenta. Cover and cement the preparation. Note the large well-defined fibres constantly branching and uniting with one another. Sketch a small part of the network. Note the existence of bundles of white fibres amongst the elastic fibres.

2. Examine a thin transverse section of ligamentum nuchæ which has been hardened in 2 per cent. solution of bichromate of potash. The section is to be stained with hæmalum and mounted in Canada balsam or dammar by the usual process, or simply in glycerine and water. Observe the grouping of the fibres and their angular shape. Sometimes the angles are rounded.

3. Pinch off the end of the tail of a dead mouse or rat, draw out the long silk-like tendons and put them into salt solution. Take one of the threads, which should be nearly three inches long, and stretch it along a slide, letting the ends dry firmly to the glass but keeping the middle part wet. Put a short piece of hair on either side and cover in salt solution. Observe with a high power the fine wavy fibrillation of the tendon. Draw. Now run dilute acetic acid (0·75 per cent.) under the cover-glass ; watch the tendon where it is becoming swollen by the acetic acid. Notice the oblong nucleated cells coming into view between the tendon-bundles. Sketch three or four cells in a row. Lastly, lift the cover-glass, wash away the acid with distilled water, place a drop of Ehrlich's hæmatoxylin or carmalum solution on the tendon, and leave the preparation until it is deeply stained ; then wash away the stain and mount the preparation in faintly acidulated glycerine.

4. Take another long piece of mouse-tendon, and after washing it in distilled water, stretch it upon a slide as before, fixing the ends by allowing them to dry on to the slide. Put a drop of nitrate of silver solution (1 per cent.) on the middle of the tendon, and leave it on for five minutes. Then wash off the silver nitrate with distilled water, and expose the slide to direct sunlight. In a very few minutes the silvered part of the tendon will be brown. As soon as this is the case, dehydrate the tendon with absolute alcohol *in situ* upon the slide, run off the alcohol, and at once put a drop of clove oil on the preparation. In a minute or two the clove oil can be replaced by xylol balsam or dammar and the preparation covered.

5. Stain, with magenta solution, a thin section of a tendon which has been hardened in 70 per cent. alcohol. Mount in dilute glycerine and cement at once.

6. For developing connective tissue study sections of the umbilical cord at different periods. Fix with formol. Stain with acid fuchsine and hæmatoxylin.

Elastic tissue is a variety of connective tissue in which the elastic fibres preponderate. It is found most characteristically in the ligamentum nuchæ of quadrupeds and the ligamenta subflava of the vertebræ, but the connective tissue of other parts may also have a considerable development of elastic fibres. It occurs in an almost pure form in the walls of the air-tubes, and uniting the cartilages of the larynx. It also enters largely into the formation of the lungs and of the walls of the blood-vessels, especially the arteries.

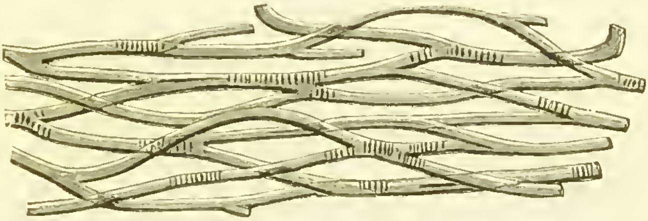

FIG. 113.—ELASTIC FIBRES FROM THE LIGAMENTUM NUCHÆ OF THE OX, SHOWING TRANSVERSE MARKINGS ON THE FIBRES.

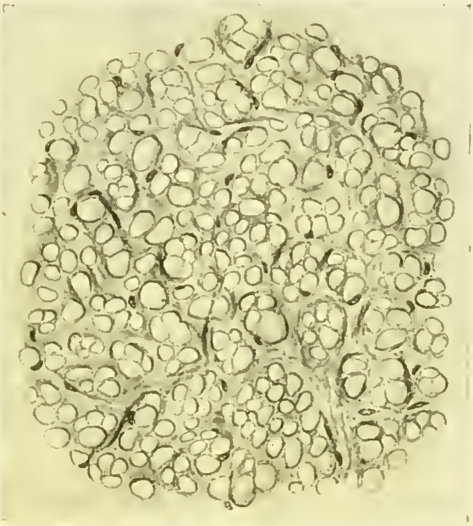

FIG. 114.—CROSS-SECTION OF ELASTIC FIBRES FROM THE LIGAMENTUM NUCHÆ OF THE OX.

The angles of the fibres are rounded in this section.

In the ligamentum nuchæ most of the fibres are very large (figs. 113, 114). They often exhibit cross markings or even transverse clefts. When dragged asunder, they break sharply across. They constantly branch and unite, so as to form a close network. In transverse section they are usually angular, but sometimes the angles are rounded off (fig. 114). They are separated into small groups or bundles (fig. 114) by intervening areolar tissue.

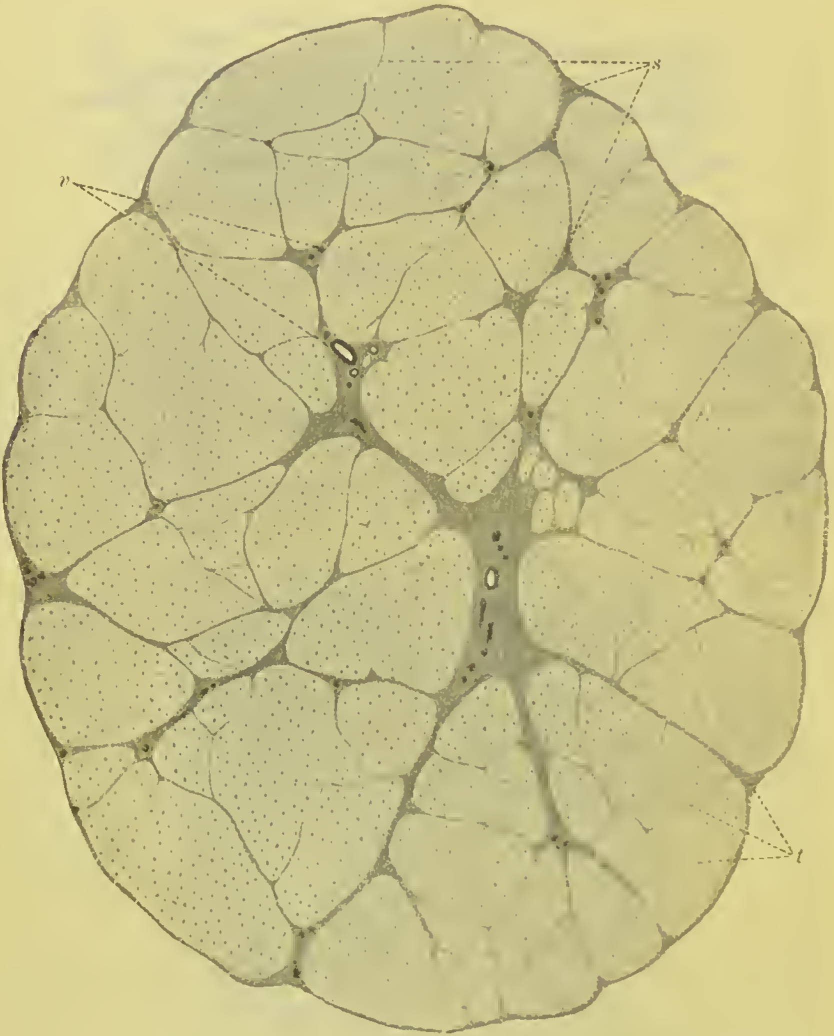

Fig. 115.—Section of tendon, human. (Sobotta.) × 32.
t, tendon-bundles; *s*, septa of areolar tissue; *v*, vessels.

Elastic tissue does not always take the form of fibres, but may occur as membranes (*e.g.* in the blood-vessels) (p. 210). Sometimes the fibres are very small, but their microscopic and chemical characters are always well marked (see p. 83).

Fibrous tissue is almost wholly made up of bundles of white fibres running in a determinate direction. These again are collected into larger bundles, which give the fibrous appearance to the tissue. The bundles are constantly uniting with one another in their course, although their component fibres remain perfectly distinct.

The interspaces between the larger bundles are occupied by areolar tissue (fig. 115, *s*; fig. 116, *c*, *d*, *e*) in which the blood-vessels and lymphatics of the fibrous tissue are conveyed. The interstices between the smallest bundles are occupied by rows of lamellar connective-tissue corpuscles (*tendon cells*), which, from being squeezed up between three or more bundles, become flattened out in two or three directions. In transverse section the cells appear somewhat stellate (fig. 116), but when seen on the flat they appear lamellar (fig. 117), and from this aspect their general shape is square or oblong. They lie, as before said, in rows between the tendon bundles, and the nuclei of adjacent cells are placed opposite one another in pairs (fig. 118). The cell-spaces correspond in general figure and arrangement to the cells which occupy them.

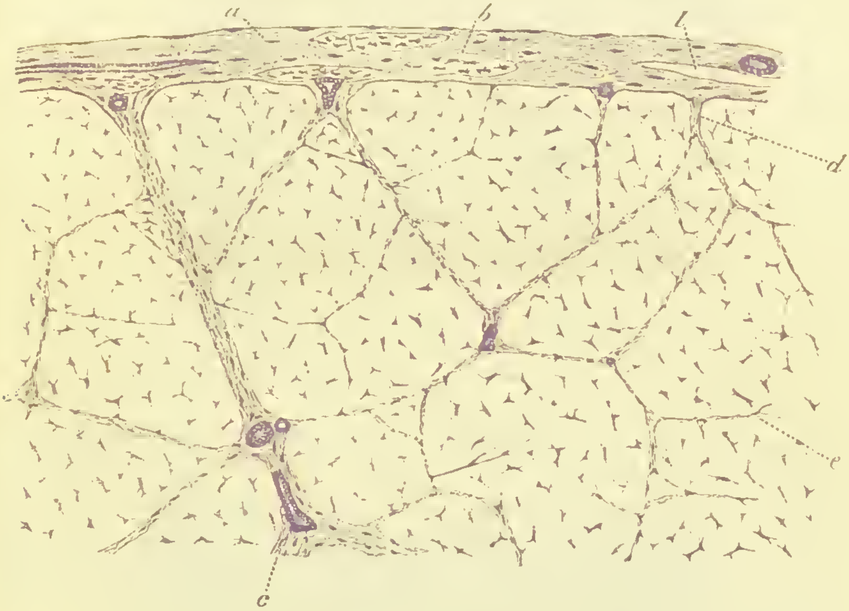

FIG. 116.—PART OF A LARGE TENDON IN TRANSVERSE SECTION. More highly magnified.

a, areolar sheath of the tendon, with the fibres for the most part running transversely; but with two or three longitudinal bundles, *b*; *l*, lymphatic cleft in the sheath; immediately over it a blood-vessel is seen cut across, and on the other side of the figure a small artery is shown cut longitudinally; *c*, large septum of areolar tissue; *d*, smaller septum; *e*, still smaller septum. The irregularly stellate bodies are the tendon-cells in section.

Fibrous tissue forms the tendons and ligaments, and also certain membranes, such as the dura mater, the fibrous pericardium, the fasciæ of the limbs, the fibrous covering of certain organs, etc. It is found wherever great strength, combined with flexibility, is concerned. It receives a few blood-vessels, disposed longitudinally for the most part, and contains many lymphatics. Both blood-vessels and lymphatics run in the areolar tissue which separates and surrounds the tendon-bundles. Tendons and ligaments also receive nerve-fibres, which, in some cases, end in localised ramifications within fusiform enlargements of the tendon-bundles (organs of Golgi), while others terminate in end bulbs or in simple Pacinian corpuscles. These will be described along with the modes of ending of nerve-fibres.

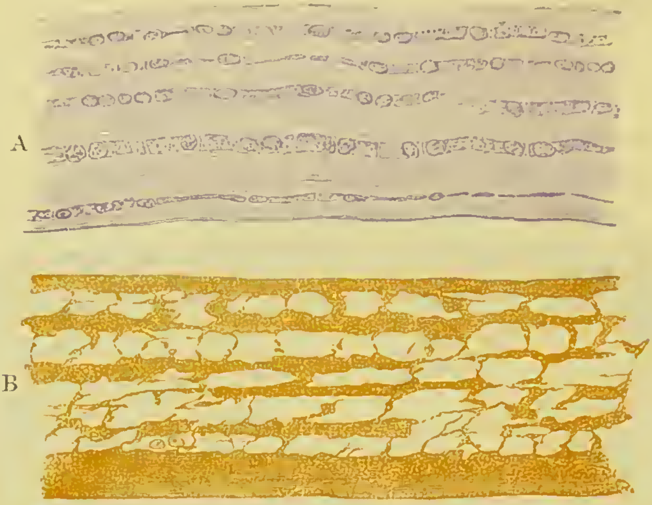

FIG. 117.—TENDONS OF MOUSE'S TAIL; SHOWING CHAINS OF CELLS BETWEEN THE TENDON-BUNDLES. 175 diameters.

A, stained with hæmatoxylin. B, stained with silver nitrate, showing the cell-spaces.

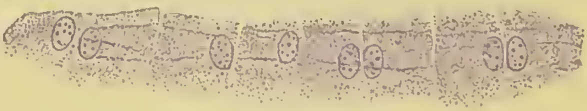

FIG. 118.—EIGHT CELLS FROM THE SAME TENDON AS REPRESENTED IN FIG. 117. A. 425 diameters.

The dark lines on the surface of the cells are the optical sections of lamellar extensions directed towards or away from the observer.

Development of connective tissue.—Connective tissue is developed in and from the cells of the mesoderm (mesenchyme) of the embryo. In those parts which are to form connective tissue, there may frequently be seen a clear space separating the cell-layers which are already formed, this clear space being permeated with fibres which appear to be produced from the cells bounding the space. Presently branching mesenchyme cells, which are budded off from the bounding cells, are found forming a syncytium within the clear space (fig. 119, *m*).

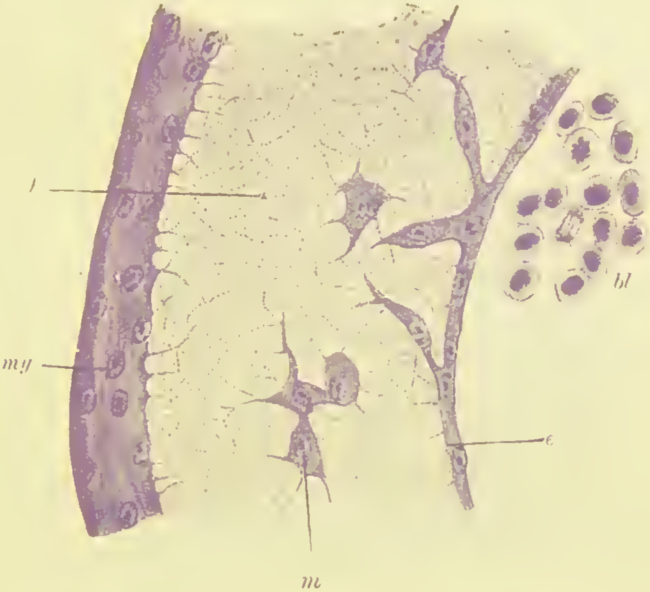

FIG. 119.—DEVELOPING CONNECTIVE TISSUE IN HEART OF CHICK-EMBRYO OF 48 HOURS. (Szily.)

my, cells forming myocardium; *j*, jelly formed of reticulum with enclosed fluid; *e*, endothelium (mesothelium) of heart; *m*, mesenchyme cells in jelly; *bl*, blood-corpuscles.

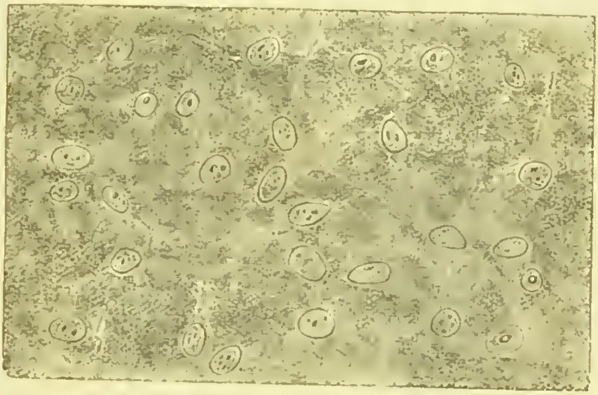

FIG. 120.—CELLS OF DEVELOPING CONNECTIVE TISSUE (MESENCHYME) UNITED TO FORM A SYNCYTIUM. (From Prenant, Bouin, and Maillard.)

No fibres are as yet developed in the intercellular substance.

In the meshes of the reticular syncytium is a muco-albuminous semifluid intercellular substance (ground-substance). The connective-tissue fibres, both white and elastic, are deposited in this ground substance, the elastic substance appearing in the form of granules (fig. 122, *g*), which subsequently become connected together into elastic fibres or laminæ, as the case may be, the white fibres appearing at first in the form of very fine bundles, which afterwards become gradually larger; so that in fibrous tissue the whole ground-substance is eventually pervaded by the bundles, and the cells of the tissue

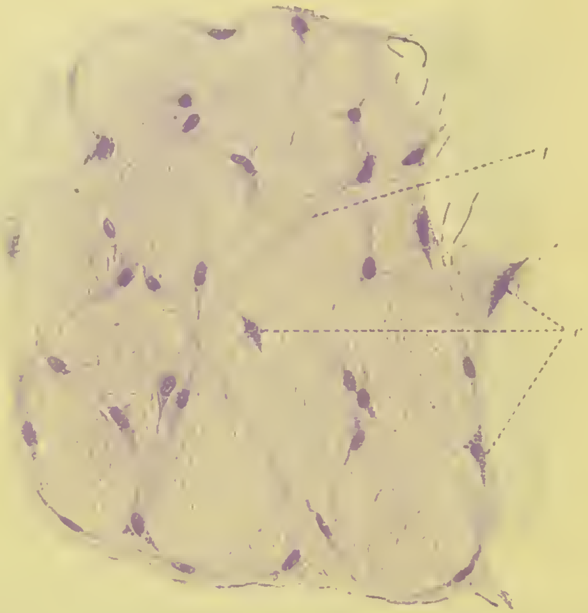

Fig. 121.—Jelly of Wharton from umbilical cord of new-born child. (Sobotta.) × 280.

f, connective-tissue fibres; *c*, cells.

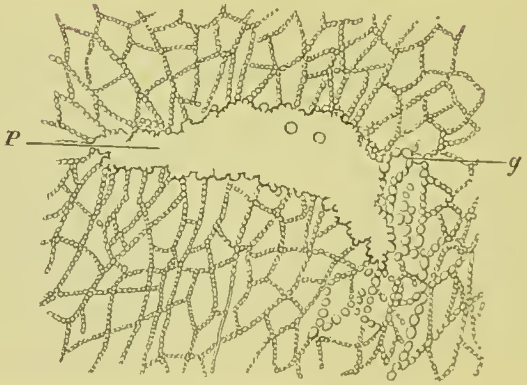

Fig. 122.—Development of elastic tissue by deposition of fine granules. (Ranvier.)

g, fibres being formed of rows of 'elastin' granules; *p*, flat plate-like expansion of elastic substance formed by the fusion of 'elastin' granules.

become squeezed up into the intervals between them. Before any considerable development of fibres has taken place, the embryonic connective tissue has a jelly-like appearance; in this form it occurs in the umbilical cord, where it is known as the *jelly of Wharton* (fig. 121).

There has been always a considerable difference of opinion as to the origin of the fibres of connective tissue, some histologists holding that they are formed within the protoplasm of the cells, which gradually lose their cell-characters as the fibres become developed within them; others taking the view that the fibres, both white and elastic, are extracellular formations. While there is no doubt that they are produced under the influence of the cells, for they first appear in close proximity to those structures, it seems on the whole probable that the fibres are deposited in the ground substance and not actually in the cell-protoplasm, so that they are rather to be looked upon, like the ground-substance itself, as formed by a process of secretion than by one of direct cell-transformation.

Mall looks upon the intercellular or ground-substance as living substance (*exoplasm*), and as bringing all the cells of the tissue into continuity. He regards the whole structure, cells and ground-substance together, as constituting a continuum, the fibres being laid down by chemical transformation in the exoplasm.

LESSON XI.

THE CONNECTIVE TISSUES (*continued*).

ARTICULAR CARTILAGE. SYNOVIAL MEMBRANES.

1. Cut two or three very thin tangential slices of the fresh cartilage of a joint, mount them in salt solution, and examine with the high power. Observe the form and grouping of the cells. Look at the thin edge of the section for spaces from which the cells have dropped out. Measure two or three cells and their nuclei, and sketch one or two groups. Now replace the salt solution by water and set the preparation aside for a little while. On again examining it, many of the cartilage cells will be found to have shrunk within their containing capsules.

2. Make other sections of the cartilage (1) from near the middle, (2) from near the edge at the attachment of the synovial membrane. Place the sections for two or three minutes in acetic acid (1 per cent.), wash them with water, and stain with dilute hæmalum or carmalum solution. When stained mount in dilute glycerine and cement the cover-glass. In (2) look for branched cartilage cells.

3. Study vertical sections of articular cartilage from an end of bone which has been fixed and decalcified, and mount the sections in glycerine and water, or, after staining with hæmalum, in dammar or xylol balsam. Sketch the arrangement of the cells in the different layers.

4. Brush a fresh joint with distilled water ; drop 1 per cent. nitrate of silver solution over it ; after five minutes wash away the nitrate of silver and expose in water to direct sunlight. When browned, place in 90 per cent. alcohol for half an hour or more, and then with a razor wetted with the same spirit cut thin sections from the surface and mount in xylol balsam or dammar after passing through clove oil. The cells and cell-spaces show white in the brown ground-substance.

5. To study the structure of the synovial membrane mount other slices from the same silvered preparation of the joint (§ 4) taken just beyond the limits of the articular cartilage, and also look for small fringed projections of the membrane. Snip them off with scissors and mount as before.

6. The superficial flexor tendons of the foot of the ox or sheep run in grooves formed by the deep flexors, and these grooves are lined, and the tendons which pass through them are covered by vaginal synovial membranes. To show the structure of these treat one of the superficial flexor tendons with silver nitrate in the manner recommended for the joint, § 4, and after hardening in 70 per cent. alcohol cut sections from the surface and mount them in balsam or dammar varnish.

Cartilage or *gristle* is a translucent bluish-white tissue, firm, and at the same time elastic, and for the most part found in connection with bones of the skeleton, most of which are in the embryo at first represented entirely by cartilage. Three chief varieties of cartilage are distinguished. In one, which is termed *hyaline*, the matrix or ground-substance is almost clear, and free from obvious fibres; in the other two, which are termed *fibro-cartilage*, the matrix is everywhere pervaded by connective-tissue fibres. When these are of the white variety, the tissue is *white fibro cartilage*; when they are elastic fibres, it is *yellow* or *elastic fibro-cartilage*.

Hyaline cartilage occurs principally in two situations—namely (1) covering the ends of the bones in the joints, where it is known as *articular cartilage*; and (2) forming the rib-cartilages, where it is known as *costal cartilage*. It also forms the cartilages of the nose, of the external auditory meatus (but not the pinna), most of those of the larynx, and the cartilages of the windpipe; in these places it serves to maintain the shape and patency of the orifices and tubes.

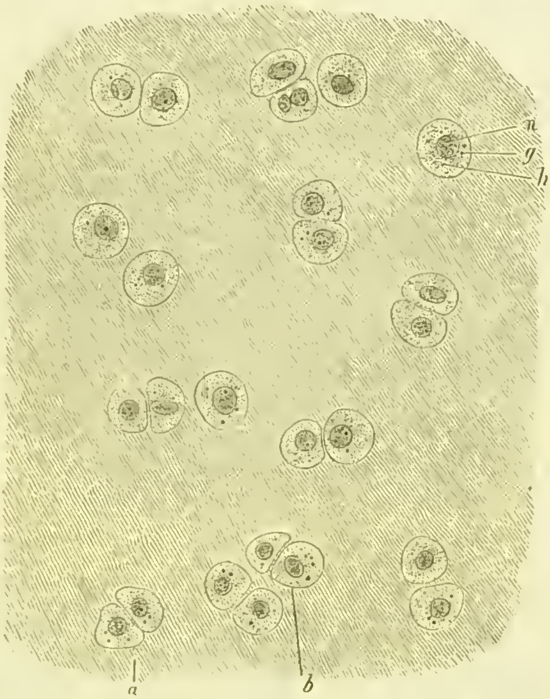

FIG. 123.—ARTICULAR CARTILAGE FROM HEAD OF METATARSAL BONE OF AMPUTATED FOOT, HUMAN (OSMIC ACID PREPARATION). THE CELL-BODIES ENTIRELY FILL THE SPACES IN THE MATRIX. 340 diameters.

a, group of two cells; *b*, group of four cells; *h*, protoplasm of cell, with *g*, fatty granules; *n*, nucleus.

Articular cartilage.—The cells of articular cartilage are generally scattered in groups of two or four throughout the matrix (fig. 123). The latter is free from obvious fibres, except at the extreme edge of the cartilage, where the connective-tissue fibres from the synovial membrane extend into it; and here also the cartilage-cells are often branched, and offer transitions to the branched connective-tissue corpuscles of that membrane (*transitional cartilage*, fig 124). By long maceration in brine, however, evidence of a fibrous structure may be obtained, even in the matrix of true hyaline cartilage. Some histologists also describe fine communications in the matrix uniting the cartilage-cells with one another, but these are of doubtful occurrence in vertebrate cartilage, although they unquestionably exist in the cartilage of cephalopods.

The matrix immediately around the cartilage-cells is often marked off from the rest by a concentric line or lines, this part of the matrix, which is the latest formed, being known as the *capsule* of the cell (fig. 128). The cells are bluntly angular in form, the sides opposite to one another in the groups being generally flattened. The protoplasm is very clear, but it may contain droplets of fat; and with a high power fine interlacing filaments and granules have been observed in it. During life the protoplasm entirely fills the cavity or cell space which it occupies in the matrix; but after death, and in consequence of the action of water and other agents, it tends to shrink away from the capsule. The nucleus is generally spherical.

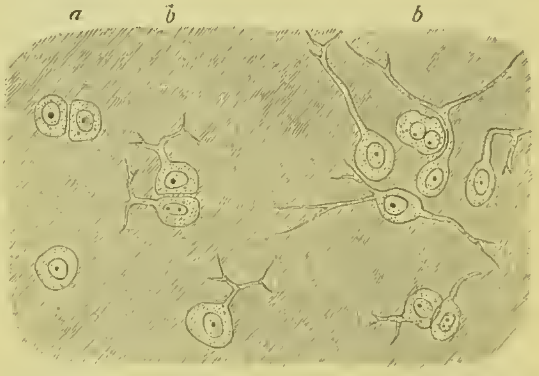

FIG. 124.—BORDER OF ARTICULAR CARTILAGE SHOWING TRANSITION OF CARTILAGE CELLS INTO CONNECTIVE-TISSUE CORPUSCLES OF SYNOVIAL MEMBRANE. FROM HEAD OF METATARSAL BONE, HUMAN. About 340 diameters.

a, ordinary cartilage-cells; *b*, *b*, with branching processes.

In vertical section (fig. 125) the deeper cell groups (*c*) are seen to be arranged vertically to the surface, the more superficial ones (*a*) parallel to the surface; whilst in an intermediate zone the groups are irregularly disposed (*b*). In the deepest part of the cartilage, next to the bone, there is often a deposit of calcareous salts in the matrix (*calcified cartilage*, *d*).

The disposition of the cells of cartilage in groups of two, four, eight, etc., is apparently due to the fact that these groups have originated from the division of a single cell first into two, and these again into two, and so on (fig. 126). The division of the cartilage-cell, like that of most other cells, is mitotic.

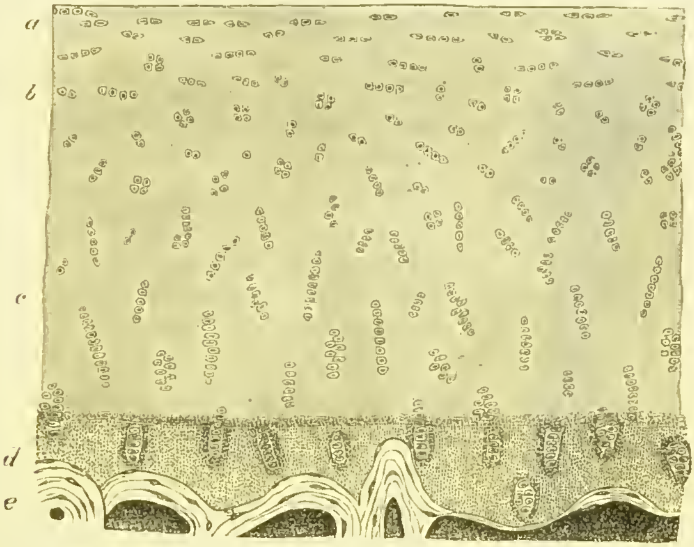

FIG. 125.—VERTICAL SECTION OF ARTICULAR CARTILAGE COVERING THE LOWER END OF THE TIBIA, HUMAN. Magnified about 30 diameters.

a, cells and cell-groups flattened conformably with the surface; *b*, cell-groups irregularly arranged; *c*, cell-groups disposed perpendicularly to the surface; *d*, layer of calcified cartilage; *e*, bone.

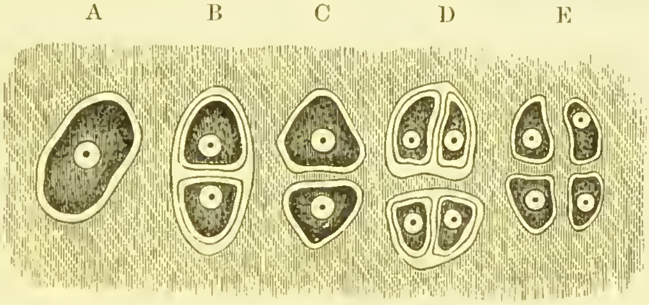

FIG. 126.—PLAN OF THE MULTIPLICATION OF CELLS OF CARTILAGE. (Sharpey.)

A, cell in its capsule; B, divided into two, each with a capsule; C, primary capsule disappeared, secondary capsules coherent with matrix; D, tertiary division; E, secondary capsules disappeared, tertiary coherent with matrix.

It would seem that the matrix is formed of successive portions, which are deposited around each cartilage-cell as the so-called 'capsules,' each newly formed portion soon blending in its turn with the previously formed matrix, whilst a new capsule is formed within it. The most newly formed portions of matrix stain with hæmatoxylin more deeply than the rest, and in some cartilages this gives the appearance of rounded balls of darkly stained matter surrounding each cell or cell-group (*chondrin-balls*, Mörner) (fig. 128).

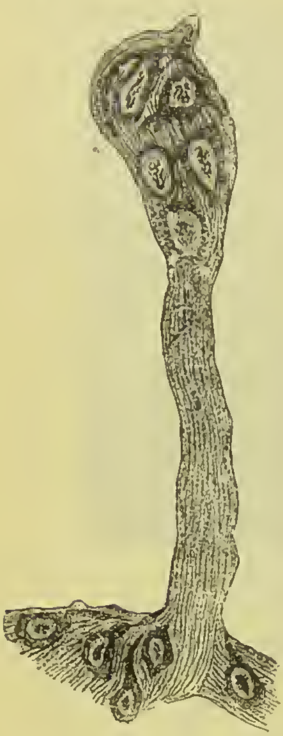

FIG. 127. — VILLUS OF SYNOVIAL MEMBRANE. (Hammar.)

Embryonic cartilage is usually characterised by the cells being sharply angular and irregular; they are even in some cases markedly branched, like those which occur at the junction of cartilage and synovial membrane in the adult. The cells are also more closely packed, the matrix being in relatively less amount than in later life.

Development.—Cartilage is formed in the embryo from mesenchyme similar to that which gives origin to other forms of connective tissue. Each cell forms a capsule around itself, and the blended capsules compose the first matrix. Cartilage sometimes remains in this condition throughout life; it is then termed *parenchymatous cartilage*. This can be seen in the mouse's ear; where also the cartilage cells become filled with fat. Cartilage at first grows partly by interstitial expansion (accompanied by cell multiplication and by formation around and between the cells of intercellular substance), partly by apposition at the perichondrium, the connective tissue becoming here transformed into cartilage At a later period of growth the increase in size and change in shape of cartilages are due almost entirely to the agency of the perichondrium.

SYNOVIAL MEMBRANES.

The **synovial membranes** are often compared with the serous membranes. They are indeed, like the latter, connective-tissue membranes which bound closed cavities moistened with fluid, but they are not connected with the lymphatic system, nor is the fluid (synovia) which moistens them of the nature of lymph. Moreover, there is either no endothelial lining, or it occurs only in patches, in place of the continuous lining which we find in the serous membranes. Long villus-like projections, simple (fig. 127) or compound—the so-called *Haversian fringes*—occur in some situations; they are beset in parts by small rounded cells, and probably serve to extend the surface for the secretion of synovia. The blood-vessels of synovial membranes are numerous, and approach close to the inner surface of the membrane. They are well seen in preparations from an injected limb.

LESSON XII.

THE CONNECTIVE TISSUES (continued).

COSTAL CARTILAGE. FIBRO-CARTILAGE.

1. Make transverse and tangential sections of a rib-cartilage, which may either be fresh, or may have been preserved in spirit or formol. Stain them with hæmalum or carmalum (if fresh, after treatment with acetic acid as in Lesson XI. § 2, or they may be placed for an hour or two in ·5 p.c. osmic acid), and mount in glycerine. Sketch a part of a transverse section under a low power under a cell-group from one of the tangential sections under a high power. Notice especially the arrangement of the cells, somewhat concentric near the surface but radial near the centre. The costal cartilages tend to become ossified near the middle in most animals, but in man when ossification occurs it is the superficial layer which is invaded.

2. Make sections of the cartilage of the external ear (pinna), either fresh or after hardening in alcohol. Mount in dilute glycerine faintly coloured with magenta or stain with orcein and mount in balsam. The upper end of the arytenoid cartilages of the ox or calf may also be employed. Notice the large reticulating elastic fibres in the matrix. Notice also the isolated granules of elastin, and around the cartilage-cell an area of clear ground-substance. If from the ear of the mouse or rat there is very little matrix and no elastic fibres, and the cells are almost in contact (parenchymatous cartilage); these cells also contain fat (staining with osmic acid).

3. Mount a section of the epiglottis in the same way. Notice the closer network of much finer fibres in its cartilage.

4. Cut sections of white fibro-cartilage (intervertebral disk or semilunar cartilage of knee), which has been hardened in picric acid followed by spirit, or in spirit only. Stain the sections with dilute hæmalum or carmalum. Mount in dilute glycerine. Observe the wavy fibres in the matrix and the cartilage-cells lying in clear areas often concentrically striated. Look for branched cartilage-cells. Sketch three or four cells and the adjoining fibrous matrix.

Costal cartilage.—In the costal cartilages the matrix is not always so clear as in the cartilages of the joints, for it more often happens that fibres become developed in it. The cells are generally larger than those of articular cartilage, and collected into larger groups (fig. 128). Near the circumference, and under the perichondrium or fibrous covering of the cartilage, they are flattened and parallel to the surface, but in the deeper parts they have a more irregular or a radiated arrangement. They frequently contain fat. The cartilages of the larynx and windpipe and of the nose resemble on the whole the costal cartilages, but the study of them may be deferred until the organs where they occur are dealt with.

Elastic or **yellow fibro-cartilage** occurs in only a few situations. These are, the cartilage of the external ear and that of the Eustachian tube, and the epiglottis and cartilages of Santorini of the larynx. The matrix is everywhere pervaded with well-defined branching fibres, which unite with one another to form a close network (figs. 129, 130).

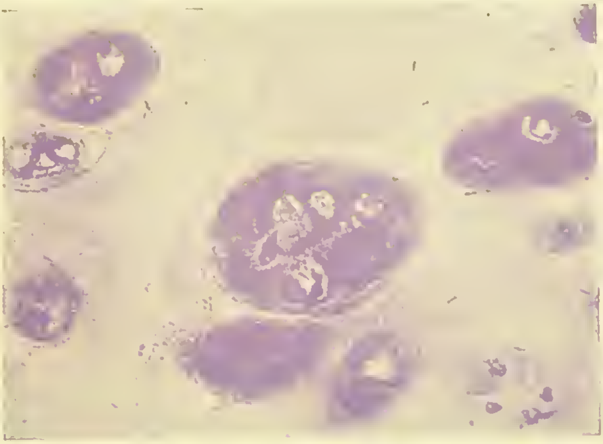

FIG. 128.—SECTION OF COSTAL CARTILAGE. Photograph. Magnified 240 diameters.

The section shows several groups of cartilage-cells. Capsule outlines are seen around the groups and also around the individual cells. The part around the cells and cell-groups is stained more than the rest of the matrix.

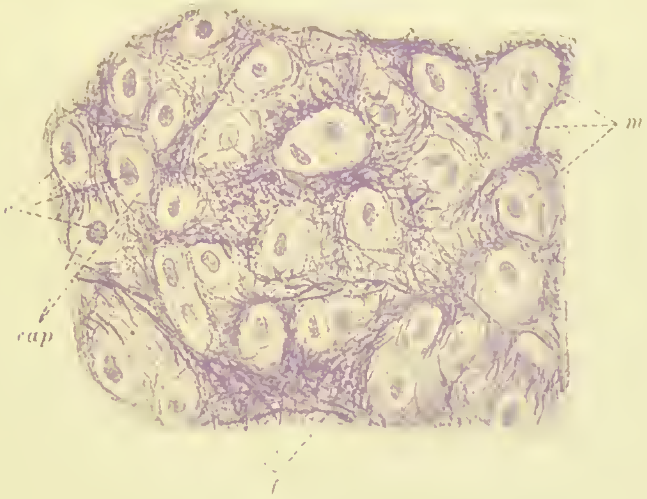

FIG. 129.—SECTION OF ELASTIC CARTILAGE OF EAR, HUMAN. (Sobotta.) × 280.

c, cartilage cells; *cap*, their capsules; *m*, clear matrix around cells and cell-groups; *f*, elastic fibres.

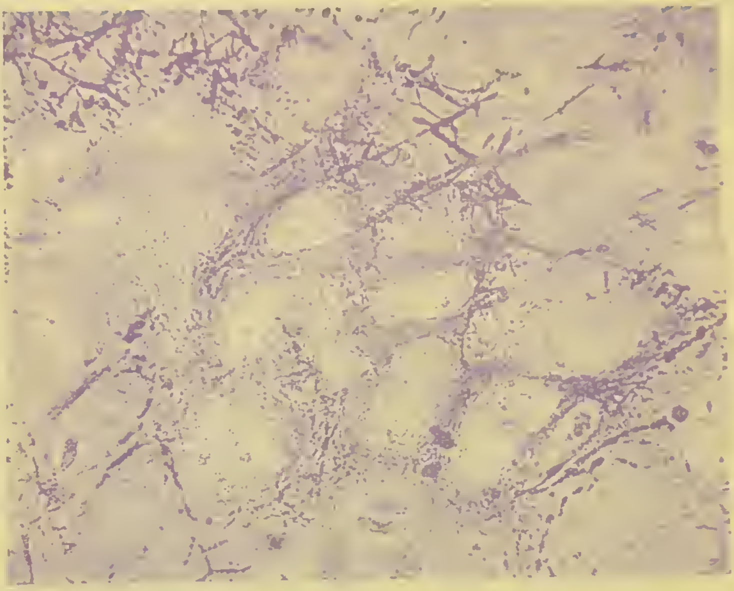

FIG. 130.—SECTION OF ELASTIC CARTILAGE (UPPER PART OF ARYTENOID OF CALF) STAINED WITH MAGENTA. Photograph. Magnified 200 diameters.

The elastin is seen partly in the form of a granular deposit, partly as finer and coarser intercommunicating fibres. These are nowhere in contact with the cartilage-cells, which are surrounded by clear cartilage-matrix. At most parts of the section the cells have dropped out, but two or three are seen still *in situ*.

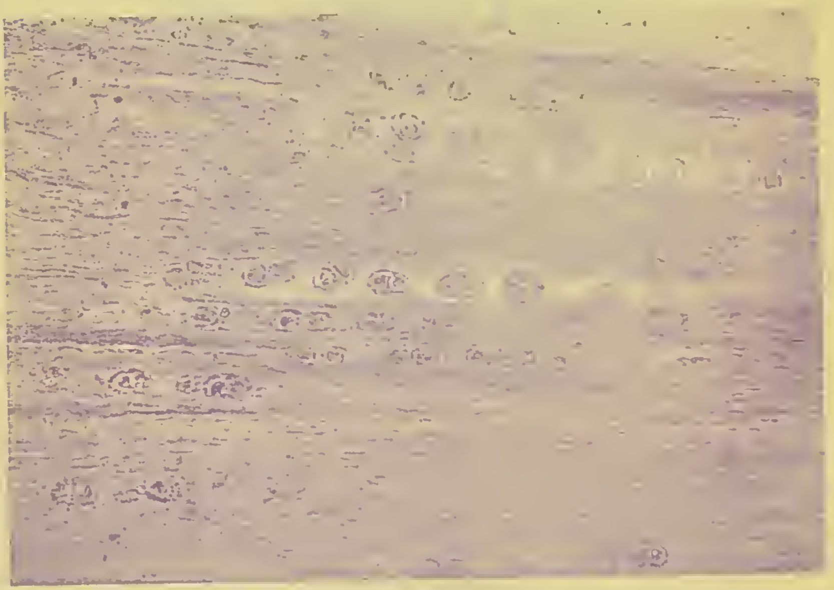

FIG. 131.—SECTION OF WHITE FIBRO-CARTILAGE. Photograph. Magnified 200 diameters.

The ground-substance is pervaded by wavy connective-tissue fibres.

These fibres resist the action of acetic acid, and are stained deeply by magenta; they are evidently elastic fibres. In the ox they are very large, but smaller in man, especially in the cartilage of the epiglottis. They appear to be developed, as with elastic tissue elsewhere (see p. 100), by the deposition of granules of elastin in the matrix, which at first lie scattered, but afterwards become joined to form the fibres.

White fibro-cartilage is found wherever great strength combined with a certain amount of rigidity is required: thus we frequently find fibro-cartilage joining bones together, as in the intervertebral disks and other symphyses. But in these cases the part in contact with the bone is always hyaline cartilage, which passes gradually into the fibro-cartilage forming the bulk of the symphysis. Fibro-cartilage is often found lining grooves in which tendons run, and it may be found in the tendons themselves. It is also employed to deepen cup-shaped articular surfaces; and in the case of the interarticular cartilages, such as those of the knee and lower jaw, to allow greater freedom of movement whilst diminishing the liability to dislocation. Under the microscope white fibro-cartilage looks very like fibrous tissue, but its cells are cartilage-cells, not tendon-cells (figs. 131, 132). They are rounded or bluntly angular and surrounded by a concentrically striated area of clear cartilage-matrix. In some parts of the intervertebral disk many of the cells are branched, and may be looked upon as transitional forms to connective-tissue corpuscles.

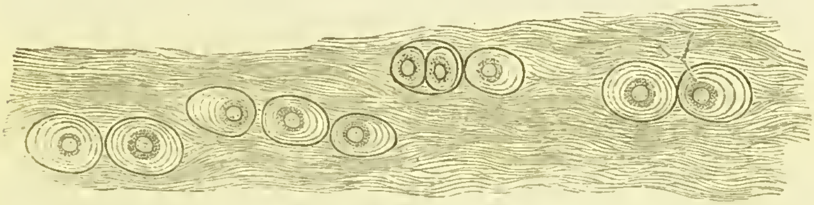

FIG. 132.—WHITE FIBRO-CARTILAGE FROM AN INTERVERTEBRAL DISK, HUMAN. Highly magnified.

The concentric lines around the cells indicate the limits of deposit of successive capsules. One of the cells has a forked process which extends beyond the hyaline area surrounding the cell, amongst the fibres of the general matrix.

LESSON XIII.

THE CONNECTIVE TISSUES (*continued*).

BONE; STRUCTURE AND DEVELOPMENT.

1. In thin sections of hard bone made by grinding,[1] observe the Haversian canals, lamellæ, lacunæ, canaliculi, etc. Make a sketch first under a low and afterwards under a high power.

2. With fine forceps strip off a thin shred from the superficial layers of a bone which has been decalcified in 5 p.c. commercial sulphurous acid and afterwards washed with water for 24 hours. It may be kept in dilute alcohol. Mount the shred in water. Observe the fibrous structure of the lamellæ. Look for perforating fibres or the holes from which they have been dragged out. Sketch a small piece of the thin edge of a lamella.

3. Stain with dilute magenta and hæmalum solution, or with methyl-blue and eosin, very thin sections of compact bone which has been fixed with 10 p.c. formol (1 to 3 days) and then decalcified in sulphurous acid as above. Mount in dilute glycerine, cementing at once. Look for fibres of Sharpey piercing the circumferential lamellæ. The elastic perforating fibres are more darkly stained than the others. Notice the stained nuclei of the bone-corpuscles in the lacunæ. In the thinnest parts of the sections try to make out the blood-vessels and other structures in the Haversian canals.

4. Mount in xylol balsam or dammar a section of a fœtal lower jaw which has been stained in bulk and embedded in paraffin.[2] Find the part where the lower jaw-bone is becoming ossified, and carefully study the appearance which it presents. The bone is prolonged in the form of osteogenic fibres which are covered with osteoblasts.

5. Intramembranous ossification may also be studied in the parietal bone of a fœtus which has been preserved in Müller's fluid. A piece of the growing edge is scraped or brushed free from its investing membranes, and from most of the cells which cover and conceal it, and is mounted in glycerine with or without previous staining with carmalum.

6. Mount in balsam or dammar sections of a fœtal limb (which may have been stained in bulk). The bones will be found in different stages of ossification, those of the digits being least developed. Make sketches illustrating the three chief stages of endochondral ossification. Notice the peculiar terminal ossification of the third phalanx.

Bone is a connective tissue in which the ground-substance is impregnated with salts of lime, chiefly phosphate, these salts constituting about two-thirds of the weight of the bone. When bones are macerated this earthy matter prevents the putrefaction of the animal matter. When bones are calcined they lose one-third of their weight,

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[1] Such a section should be purchased.

[2] See Appendix for method of staining in bulk. In place of this the sections may be stained by Mallory's method, which brings out the osteogenic fibres.

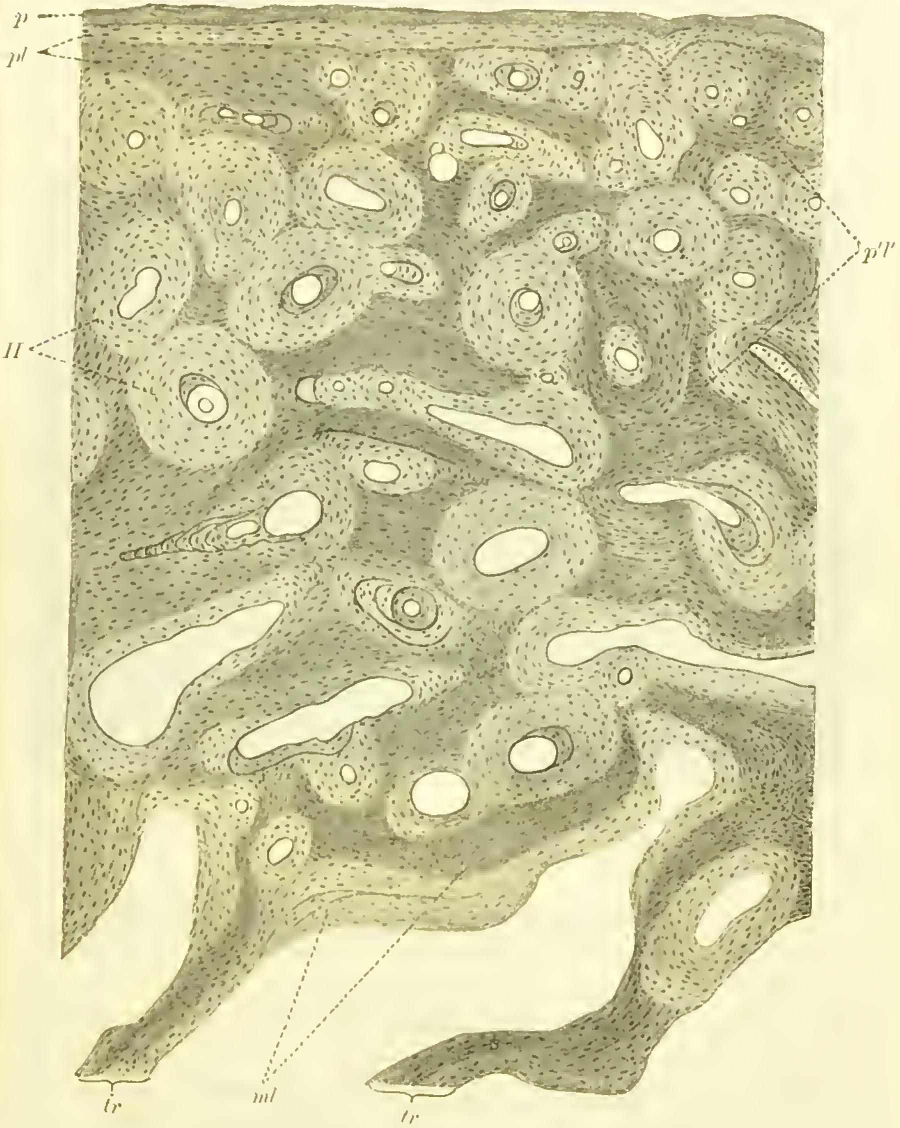


FIG. 133.—SECTION OF A DECALCIFIED HUMAN RADIUS. (Sobotta.) × 48.

p, periosteum; *pl*, periosteal bony lamellæ; *p'l'*, deeply seated lamellæ between the Haversian systems; *H*, Haversian systems; *tr*, *tr*, trabeculæ of spongy substance; *ml*, lamellæ bounding medullary spaces.

owing to the destruction of the animal matter; when steeped in acid the earthy salts are dissolved and only the animal matter is left. This, like areolar and fibrous tissue, is converted into gelatine by boiling.

Bony tissue is either *compact* or *cancellated*. Compact bone is dense, like ivory; cancellated is spongy with obvious interstices. The outer layers of all bones are compact, and the inner part is generally cancellated, but the shaft of a long bone is almost entirely made up of compact substance, except along the centre, which is hollow and filled with marrow. The interstices of cancellated bone are also occupied by marrow. Externally bones are covered except at the joints by a vascular fibrous membrane, the *periosteum*.

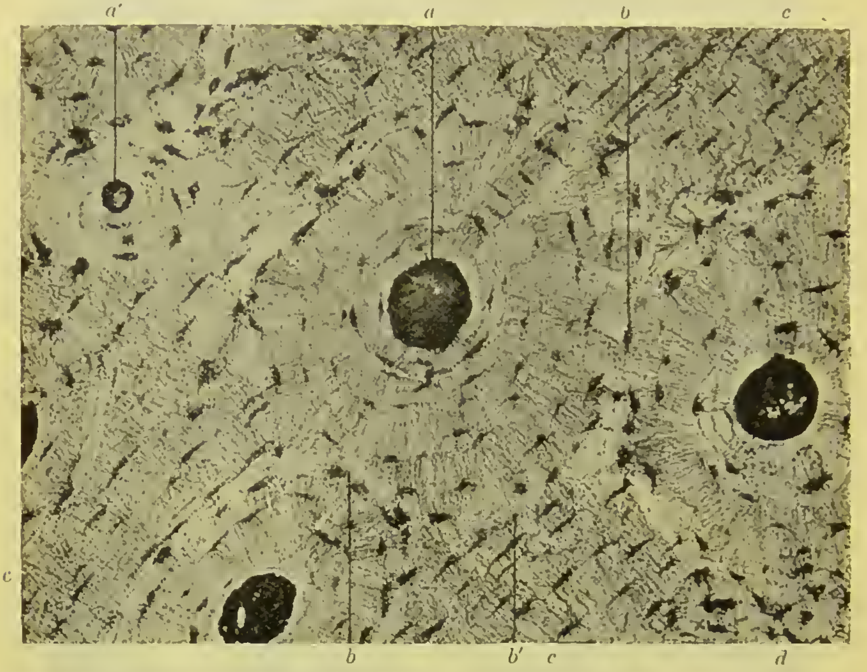


FIG. 134.—PHOTOGRAPH OF TRANSVERSE SECTION OF COMPACT BONE, MADE BY GRINDING, SHOWING THREE HAVERSIAN CANALS WITH THEIR CONCENTRIC LAMELLÆ, AND ALSO INTER-HAVERSIAN BONY SUBSTANCE. Magnified 200 diameters.

a, Haversian canal, filled with air and débris; *a'*, a very small canal; *b*, *b*, junction of two Haversian systems; *b'*, margin of Haversian system abutting on inter-Haversian lamellæ; *c*, *c*, *c*, lamellæ parallel to periosteum; *d*, inter-Haversian bone with irregular lacunæ.

True bone is always made up of *lamellæ*, and these again are composed of fine *fibres* lying in a *calcified ground-substance*. Between the lamellæ are branched cells, the *bone-corpuscles*, which lie in cell spaces or *lacunæ*. The ramified passages which contain the cell-processes are termed *canaliculi*.

In cancellated bone the blood-vessels run in the interstices supported by the marrow. In compact bone they are contained in little canals—the *Haversian canals*—which everywhere pervade the bone. These canals are about 0·05 mm. ($\frac{1}{500}$ inch) in diameter, but some are smaller, others larger than this. Their general direction is longitudinal, *i.e.* parallel to the long axis of the bone, but they are constantly united by transversely and obliquely running passages. In a section across the shaft of a long bone they are seen as small rounded or irregular holes (fig. 133). When the section has been made by grinding, the holes get filled up with air and debris, and they then look black by transmitted light, as do also the lacunæ and canaliculi (figs. 134, 135). Most of the lamellæ in compact bone are disposed concentrically around the Haversian canals; they are known as the Haversian lamellæ, and with the included canal form what is known as a *Haversian system.* The lacunæ of Haversian system communicate with one another and with the Haversian canal, but not as a rule with the lacunæ of adjacent Haversian systems. The angular interstices between the Haversian systems are generally occupied by bony substance which is fibrous but not lamellar (figs. 134, 135, *d*). Besides the lamellæ of the Haversian systems there is a certain thickness of bone at the surface, immediately underneath the

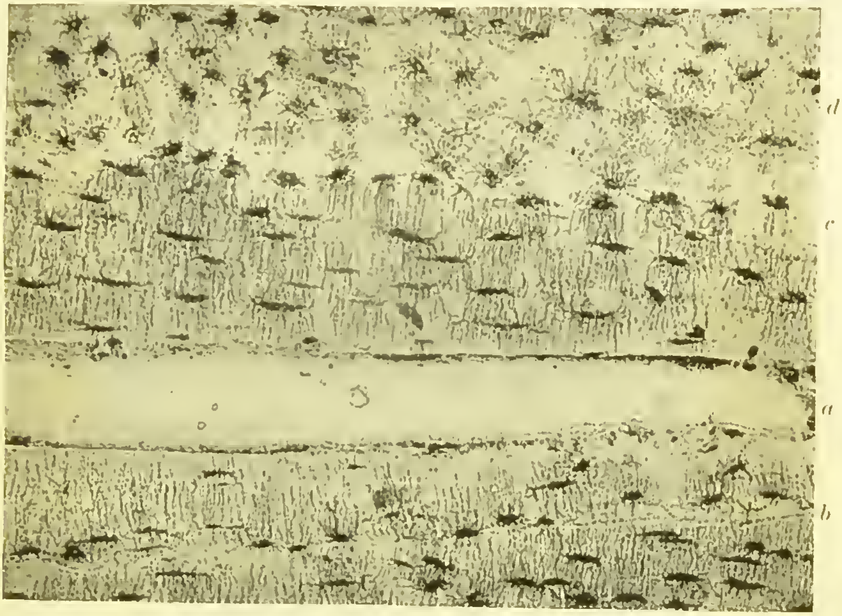


FIG. 135.—LONGITUDINAL SECTION OF COMPACT BONE, SHOWING HAVERSIAN SYSTEMS OF LAMELLÆ, AND INTER-HAVERSIAN BONE. Magnified 200 diameters.

a, Haversian canals cut longitudinally; *b*, junction of two Haversian systems of lamellæ; *c*, margin of Haversian system abutting upon inter-Haversian bone with irregular lacunæ, *d*.

periosteum, which is composed of lamellæ arranged parallel with the surface; these are the *circumferential* or *periosteal lamellæ* (fig. 133, *pl*). They are pierced here and there by simple canals for blood-vessels, the so-called *Volkmann's canals*, which are proceeding from the periosteum to join the system of Haversian canals, and also by calcified bundles of white fibres and by elastic fibres which may also be prolonged from the periosteum. These are the *perforating fibres of Sharpey* (fig. 136).

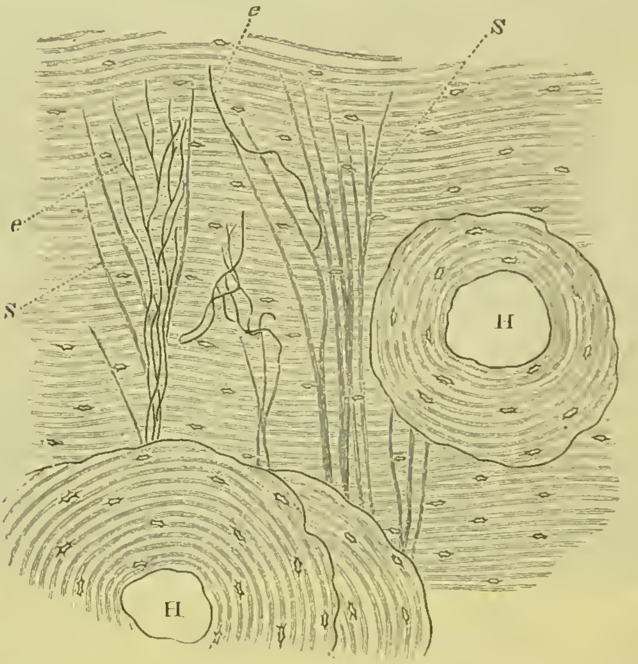


FIG. 136.—TRANSVERSE SECTION OF DECALCIFIED HUMAN TIBIA, FROM NEAR THE SURFACE OF THE SHAFT.

H, H, Haversian canals, with their systems of concentric lamellæ; in all the rest of the figure the lamellæ are circumferential; *s*, *s*, ordinary perforating fibres of Sharpey: *e*, *e*, elastic perforating fibres. Drawn under a power of about 150 diameters.

The lamellæ of bone are fibrous in structure. This may be seen in shreds torn off from the superficial layers of a decalcified bone (fig. 137). The fibres (*decussating fibres of Sharpey*, *lamella-fibres*) often cross one another in adjacent lamellæ, and in the Haversian systems they run in some lamellæ concentrically, in others parallel with the Haversian canal. In shreds of lamellæ which have been peeled off from the surface the perforating fibres may sometimes be seen projecting from the surface of the shred, having been torn out of the deeper lamellæ (fig. 137, *c*, *c*). When tendons or ligaments are inserted into bone, their bundles of white fibres are prolonged into the bone as perforating fibres.

The lacunæ are occupied by nucleated corpuscles, which send branches along the canaliculi (fig. 138). They have a special lining layer different in chemical composition from the rest of the bone, being much more resistant to the action of strong chemical solvents such as hydrochloric acid (Neumann). The dentinal tubules of the teeth have a similar lining layer.

The Haversian canals contain one or two blood-capillaries and nervous filaments, besides a little connective tissue; and the larger ones may also contain a few marrow-cells. There are also cleft-like lymphatic spaces running with the vessels, their cells being connected through canaliculi with branches from corpuscles within the neighbouring lacunæ of the osseous substance (fig. 139).

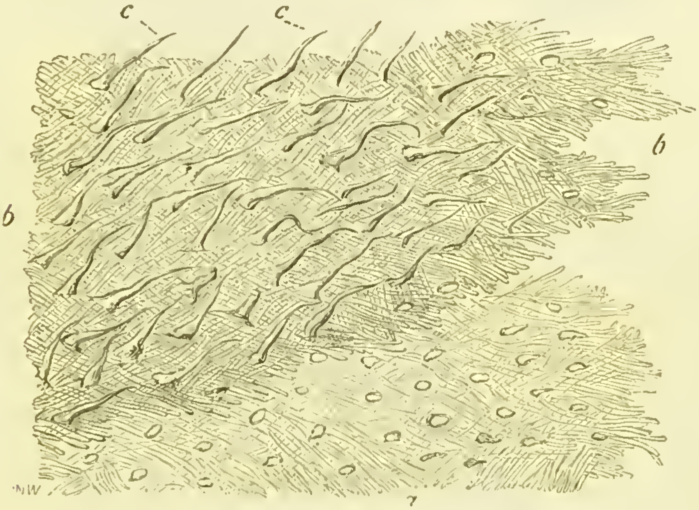


FIG. 137.—LAMELLÆ TORN OFF FROM A DECALCIFIED HUMAN PARIETAL BONE AT SOME DEPTH FROM THE SURFACE. (Sharpey.)

a, lamellæ, showing decussating fibres; *b*, *b*, thicker part, where several lamellæ are superposed; *c*, *c*, perforating fibres; the fibrils which compose them are not shown in the figure. Apertures through which perforating fibres had passed are seen, especially in the lower part, *a*, of the figure. Magnitude as seen under a power of 200 diameters, but not drawn to scale. (From a sketch by Allen Thomson.)

The **periosteum** may be studied in torn-off shreds, in preparations stained *in situ* with silver nitrate, and in stained sections from an unmacerated bone which has been decalcified. It is a fibrous membrane composed of two layers, the inner of which contains many elastic fibres. In the outer layer numerous blood-vessels ramify and send branches to the Haversian canals of the bone. The periosteum ministers to the nutrition of the bone, partly on account of the blood-vessels and lymphatics it contains, partly, especially in young animals, on account of the existence between it and the bone of a layer of *osteoblasts* or *bone-forming cells*, a remainder of those which originally produced the bone. It also serves to give attachment to muscular fibres.

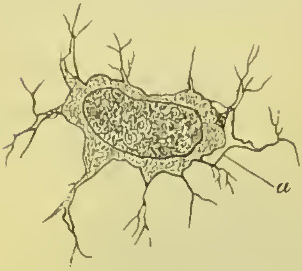


FIG. 138.—A BONE-CELL ISOLATED AND HIGHLY MAGNIFIED. (Joseph.)

a, proper wall of the lacuna (Neumann's layer), where the corpuscle has shrunken away from it.

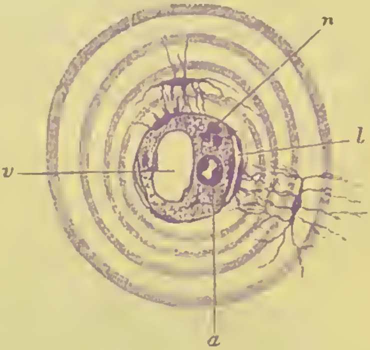


FIG. 139.—SECTION OF A HAVERSIAN CANAL, SHOWING ITS CONTENTS. Highly magnified.

a, small arterial capillary vessel; *v*, large venous capillary; *n*, pale nerve-fibres cut across; *l*, cleft-like lymphatic vessel; one of the cells forming its wall communicates by fine branches with the branches of a bone-corpuscle. The substance in which the vessels run is connective tissue with ramified cells; its finely granular appearance is probably due to the cross-section of fibrils. The canal is surrounded by several concentric lamellæ.

The **marrow** of bone has been already studied (pp. 43 to 46).

DEVELOPMENT OF BONE.

True bone is formed in all cases by ossification of connective tissue. Sometimes the bone is preceded by cartilage, which first becomes calcified, and this is then invaded, and for the most part removed, by an embryonic connective tissue which re-deposits bony matter in the interior of the cartilage. This is *intracartilaginous* or *endochondral ossification*. At the same time layers of bone are being formed outside the cartilage underneath the periosteum. The whole bone thus formed is termed a *cartilage-bone*. Sometimes the bone is not preceded by cartilage, and then the only process which occurs is one corresponding to the subperiosteal ossification of the cartilage bone; the ossification is then known as *intramembranous*, and the bone formed is a *membrane-bone*.

Ossification in cartilage.—This may be described as occurring in three stages. In the *first stage* the cells in the middle of the cartilage become enlarged and arranged in rows radiating from the centre (fig. 140), and fine granules of calcareous matter are deposited in the matrix. Simultaneously with this the osteoblasts underneath the periosteum deposit a layer or layers of fibrous lamellæ upon the

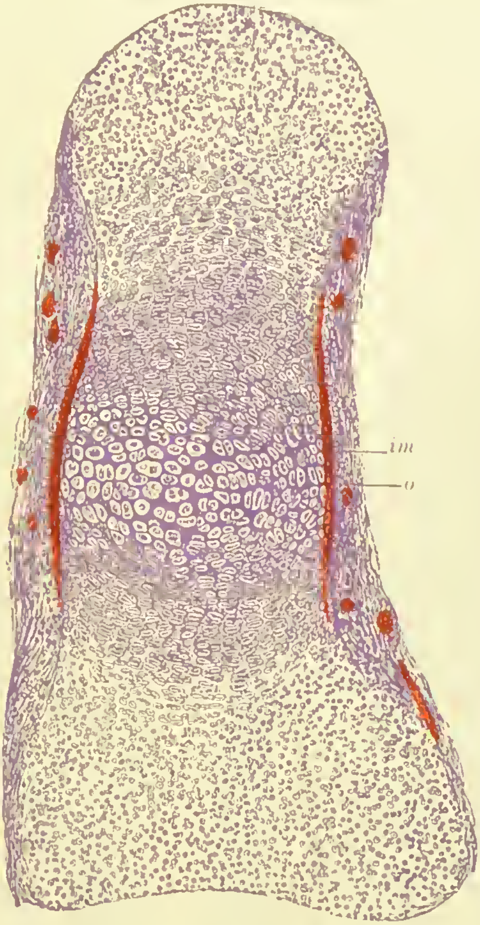


FIG. 140.—SECTION OF PHALANGEAL BONE OF HUMAN FOETUS AT THE TIME OF COMMENCING OSSIFICATION. (From a preparation by F. A. Dixey.) The preparation was stained in bulk with magenta. The drawing is made from a photograph, and is magnified about 75 diameters.

The cartilage cells in the centre are enlarged and are separated from one another by stained calcified matrix: *im*, layer of bone deposited underneath the periosteum; *o*, layer of osteoblasts by which the layer has been formed. Some of the osteoblasts are already embedded in the new bone as bone-cells within lacunæ. The cartilage-cells are flattened and arranged in rows above and below the calcified centre. At the ends of the cartilage the cells are small, and the groups are irregularly arranged; the fibrous periosteum is not sharply marked off from the cartilage.

surface of the cartilage, and these lamellæ also become calcified (fig. 140, *im*). As they are formed, some of the osteoblasts (*o*) are included between them and become bone-corpuscles.

In the *second stage* some of the subperiosteal tissue eats its way through the newly formed layer of bone and into the centre of the calcified cartilage (fig. 141, *ir*). This is freely absorbed before it (fig. 143), so that large spaces are produced which are filled with osteoblasts, and contain numerous blood-vessels which have grown in at the same time. These spaces are termed *medullary spaces*, and this second stage may be termed the *stage of irruption*.

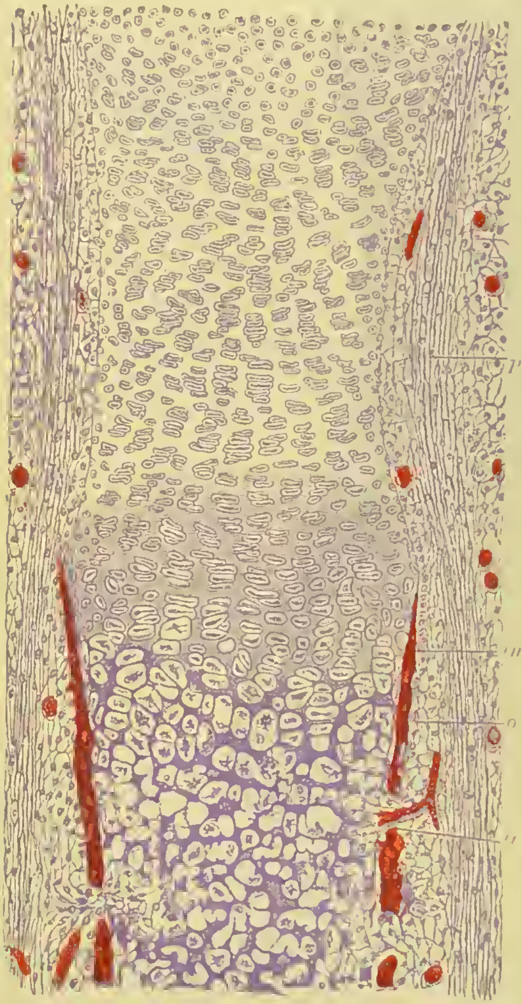


FIG. 141.—SECTION OF PART OF ONE OF THE LIMB-BONES OF A FŒTAL CAT, AT A MORE ADVANCED STAGE OF OSSIFICATION THAN IS REPRESENTED IN FIG. 140, AND SOMEWHAT MORE HIGHLY MAGNIFIED. Drawn from a photograph.

The calcification of the cartilage-matrix has advanced from the centre, and is extending between the groups of cartilage-cells, which are arranged in characteristic rows. The subperiosteal bony deposit (*im*) has extended *pari passu* with the calcification of the cartilage-matrix. The cartilage cells in the calcified part are mostly shrunken and stellate; in some cases they have dropped out of the spaces. At *ir* and in two other places an irruption of the subperiosteal tissue, composed of ramified cells with osteoblasts and growing blood-vessels, has penetrated the subperiosteal bony crust, and has begun to excavate secondary areolæ or medullary spaces; *p*, fibrous layer of the periosteum; *o*, layer of osteoblasts, some of them are embedded in the osseous layer as bone-corpuscles in lacunæ. The blood-vessels are occupied by blood-corpuscles. Beyond the line of ossific advance the periosteum may be noticed to be distinctly incurved. This incurvation is gradually moved on, the cartilage expanding behind it until the head of the bone is reached, when it forms the periosteal notch or groove represented in figs. 141 and 147.

In the *third stage* of endochondral ossification there is a gradual advance of the ossification towards the extremities of the cartilage, and at the same time a gradual deposition of fresh bony lamellæ and spicules on the walls of the medullary spaces, and on the surface of the new bone under the periosteum. The advance into the cartilage always takes place by a repetition of the same changes, the cartilage-cells first enlarging and becoming arranged in rows, the matrix between the rows becoming calcified, and then the calcified cartilage becoming excavated from behind by the osteoblastic tissue so as to form new medullary spaces (fig. 142). The walls of these are at first formed only by remains of the calcified cartilage-matrix (fig. 142, *c*), but they soon become thickened by lamellæ of fibrous bone which are deposited by the osteoblasts, and between which bone-corpuscles become included, as in the case of the subperiosteal bone. The latter advances *pari passu* with the endochondral calcification, but beyond this the uncalcified cartilage grows both in length and breadth, so that the ossification is always advancing into larger portions of cartilage; hence the endochondral bone as it forms assumes the shape of an hour-glass, the cylindrical shape of the shaft being maintained by additions of periosteal bone to the outside (see fig. 144). The absorption of the

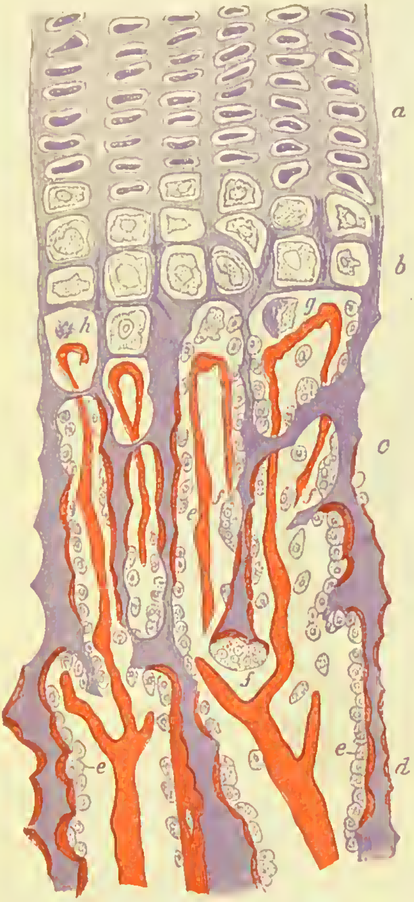


FIG. 142.—PART OF A LONGITUDINAL SECTION OF THE DEVELOPING FEMUR OF THE RABBIT. (Klein.) Drawn under a magnifying power of 350 diameters.

a, rows of flattened cartilage-cells; *b*, greatly enlarged cartilage-cells close to the advancing bone, the matrix between is partly calcified; *c*, *d*, already formed bone, the osseous trabeculæ being covered with osteoblasts (*e*) except here and there, where an osteoclast (*f*) is seen eroding parts of the trabeculæ; *g*, *h*, cartilage-cells which have become shrunken and irregular in shape. From the middle of the figure downwards the trabeculæ, which are formed of calcified cartilage-matrix, are becoming covered with secondary osseous substance deposited by the osteoblasts. The vascular loops at the extreme limit of the bone are well shown, as well as the abrupt disappearance of the cartilage-cells.

calcified cartilage matrix appears to be effected, as is the case with absorption of bony matter wherever it occurs, by large multi-nucleated cells (fig. 142, *f*, *f*) which are termed *osteoclasts.* They are multi-nucleated giant cells like those of the marrow, and are always found on surfaces where absorption of bone is taking place, whereas the osteoblasts are always found covering surfaces where bony deposit is proceeding (fig. 145).

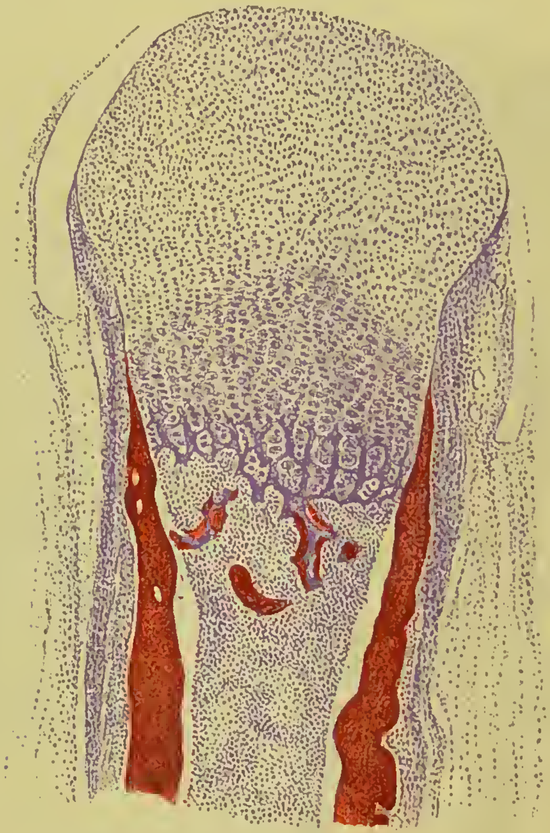


FIG. 143.—LONGITUDINAL SECTION THROUGH PART OF A PHALANX OF A SIX MONTHS' HUMAN EMBRYO. (Kölliker.)

The calcified cartilage is completely absorbed almost to the limit of advancing calcification. The osseous substance on either side is periosteal bone. The embryonic marrow has shrunk somewhat away from it.

The bone which is first formed is more reticular and less regularly lamellar than that of the adult, and contains no Haversian systems. The regular lamellæ are not deposited until some little time after birth, and their deposition is generally preceded by a considerable amount of absorption. It is about this time also that the medullary canal of the long bones is formed by the absorption of the bony tissue which originally occupies the centre of the shaft.

After a time the cartilage in one or both ends of the long bones begins to ossify independently, and the *epiphyses* are formed (fig. 148).

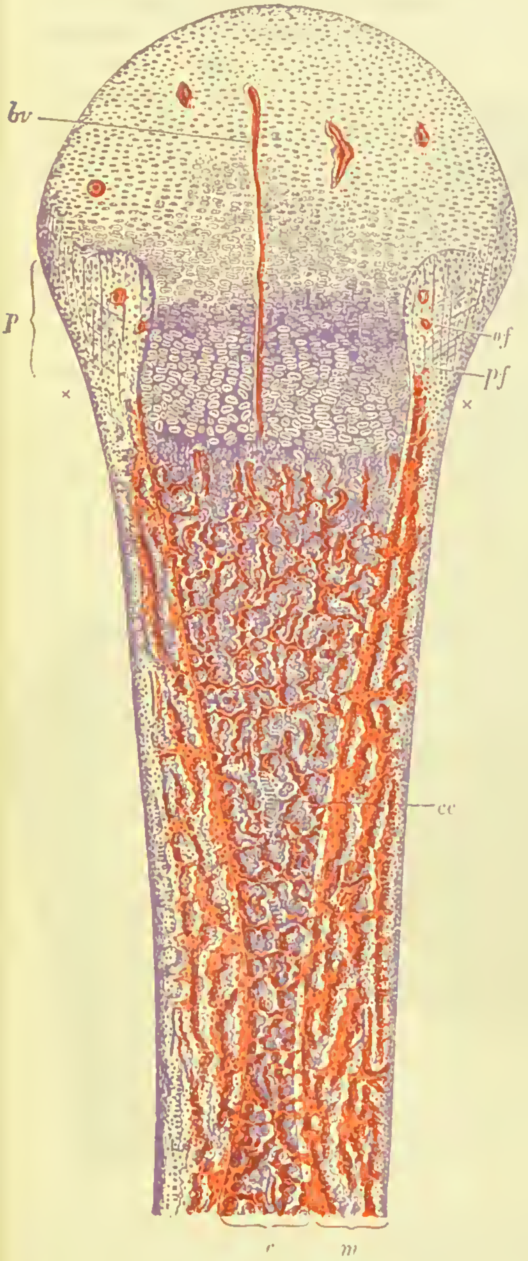


FIG. 144.—LONGITUDINAL SECTION THROUGH THE UPPER HALF OF THE DECALCIFIED HUMERUS OF A FŒTAL SHEEP, AS SEEN UNDER A MAGNIFYING POWER OF ABOUT 30 DIAMETERS.

c, the part of the shaft which was primarily ossified in cartilage; what remains of the primary bone is represented dark, enveloped by the clear secondary deposit. The areolæ of the bone are occupied by embryonic marrow with osteoblasts, and blood-vessels variously cut. One long straight vessel (*bv*) passes in advance of the line of ossification far into the cartilaginous head, most of the others loop round close to the cartilage. At one or two places in the older parts of the bone elongated groups of cartilage-cells (*cc*) may still be seen, which have hitherto escaped absorption. *m*, the part of the bone that has been ossified in membrane, that is to say, in the osteoblastic tissue under the periosteum. It is well marked off from the central portion, and is bounded, peripherally, by a jagged edge, the projections of which are indistinctly seen to be prolonged by bunches of osteogenic fibres. A row of osteoblasts covers the superficial layer of the bone. The subperiosteal layer is prolonged above into the thickening (*p*) which encroaches upon the cartilage of the head of the bone, and in which are seen amongst numerous osteoblasts and a few blood-vessels, the straight longitudinal osteogenic fibres (*of*), and some other fibres (*pf*) crossing them, and perhaps representing fibres of Sharpey. The calcareous salts having been removed by an acid, the granular nature of the ossific deposit between the rows of cartilage-cells is not seen in this specimen; it would have extended as far as a line joining the marks × ×. Observe the general tendency of the osseous trabeculæ and the vascular channels between them to radiate from the original centre of ossification. This is found to prevail more or less in all bones when they are first formed, although the direction of the trabeculæ may afterwards become modified in relation with varying physiological conditions, and especially as the result of pressure in different directions.

These are not joined to the shaft until the growth of the bone is completed. Growth takes place *in length* by an expansion of the cartilage which intervenes between the shaft and the epiphyses (*intermediate cartilage*), and by the gradual extension of the ossification into it; *in width* entirely by the deposition of fresh bony layers under the periosteum. In the terminal phalanges of the digits the ossification starts, not from the middle of the cartilage, but from its distal extremity (Dixey).

For the regeneration of portions of bone which have been removed by disease or operation it is important that the periosteum be left, because a considerable amount of the blood supply comes through the vessels of the periosteum, and there are also osteoblasts on its under surface. But fragments of bone may under some circumstances undergo regeneration even after removal

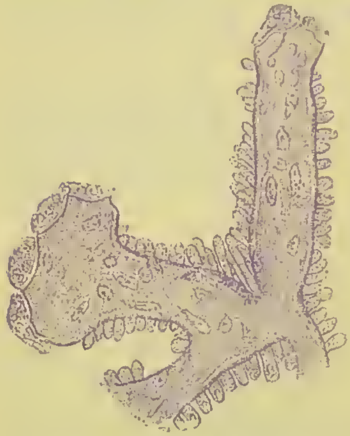


FIG. 145.—BONY TRABECULÆ FROM THE DEVELOPING LOWER JAW OF A CALF, SHOWING OSTEOCLASTS AT THE EXTREMITIES WHERE ABSORPTION IS PROCEEDING, AND OSTEOBLASTS COVERING THE SIDES WHERE DEPOSITION OF BONE IS GOING ON. (Kölliker.)

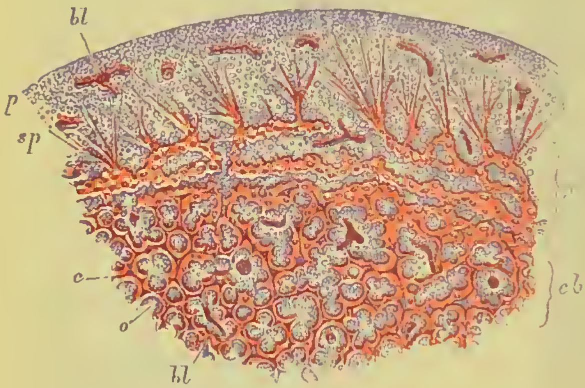


FIG. 146.—TRANSVERSE SECTION OF A DEVELOPING BONE, SHOWING THE PERIOSTEAL LAYER BECOMING FORMED FROM OSTEOGENIC FIBRES.

cb, cartilage bone; *pb*, periosteal bone; *sp*, bone spicules prolonged by osteogenic fibres; *p*, periosteum; *bl*, blood-vessels; *c*, remains of the calcified cartilage; *o*, osteoblasts forming bone upon this.

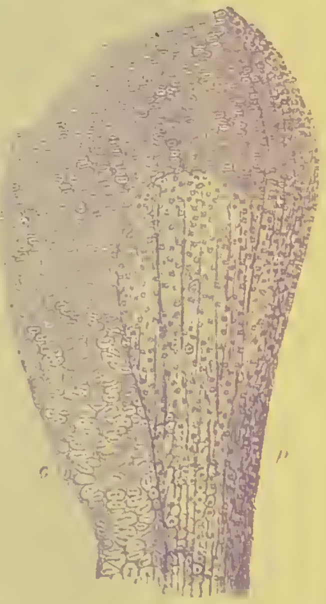


FIG. 147.—SECTION OF THE OSSIFICATION GROOVE IN THE HEAD OF A LONG BONE.

c, cartilage; *p*, periosteal tissue with osteogenic fibres and osteoblasts. This tissue occupies the "groove."

of the periosteum, by the agency of the osteoblasts and vessels in the marrow.

Intramembranous ossification.—In this variety of ossification (figs. 149, 150), the bone is not preceded by cartilage at all, and therefore no

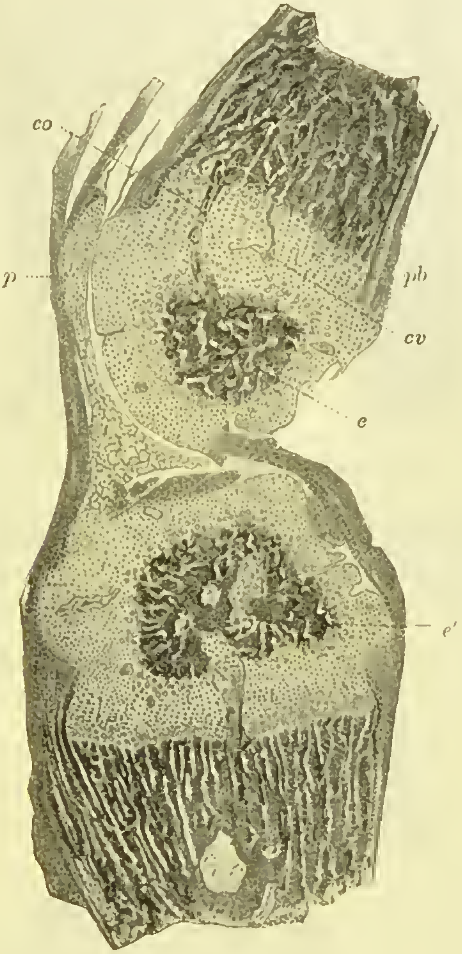


FIG. 148.—SECTION THROUGH KNEE-JOINT OF EIGHT-DAY RABBIT DURING THE FORMATION OF EPIPHYSES. (A. Bidder.)

co, canal carrying osteoblastic tissue from the diaphysis of the femur to its epiphysis; *cv*, vascular canal in cartilage; *pb*, periosteal bone; *e*, epiphysis in end of femur; *e'*, epiphysis in head of tibia, containing an island of unossified cartilage; *p*, patella, still cartilaginous.

endochondral bone is formed, but the calcification occurs in a sort of embryonic connective tissue which contains numerous osteoblasts and blood-vessels. The fibres of this tissue (osteogenic fibres), which, like those of fibrous tissue, are collected into small bundles, become enclosed in a

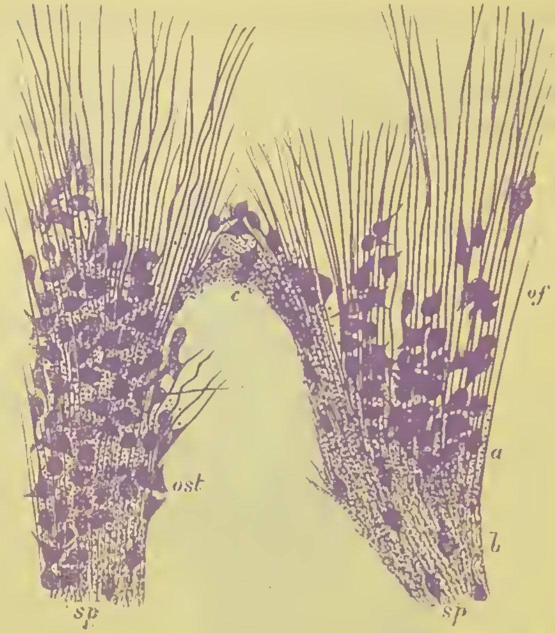


FIG. 149.—PART OF THE GROWING EDGE OF THE DEVELOPING PARIETAL BONE OF A FŒTAL CAT, 1½ INCH LONG.

sp, bone spicules, with some of the osteoblasts embedded in them, producing the lacunæ; *of*, osteogenic fibres prolonging the spicules, with osteoblasts (*ost*) between them and applied to them; *a*, granular calcific deposit occurring in the ground-substance between the fibres; *c*, union of two adjacent spicules.

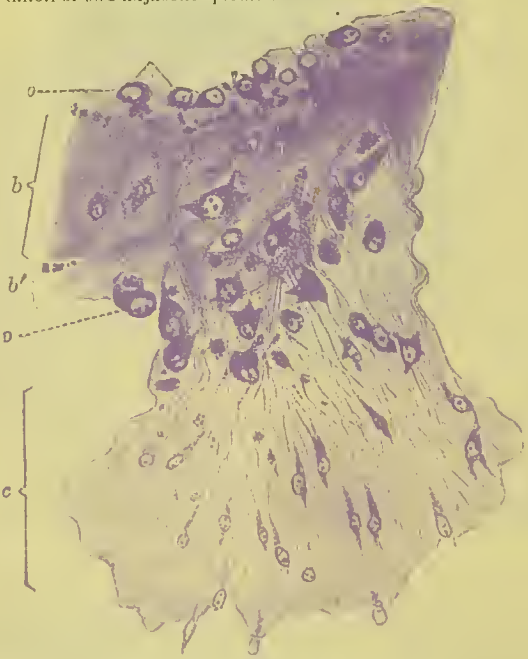


FIG. 150.—SECTION OF OSSIFYING MAXILLARY BONE OF NEW-BORN RAT. (v. Korff.)

o, o, osteoblasts; *b*, bony substance with osteoblasts and fibres; *b'*, growing border of bone; *c*, embryonic connective tissue, showing its fibres continuous with the osteogenic fibres of the growing border.

calcareous matrix, produced by the deposition of lime salts in the ground-substance of the connective tissue; and as the fibres grow, the calcification extends further and further, so that bony spicules are formed, which, as they become thickened, run together to form reticular layers, leaving spaces filled with osteoblasts around the blood-vessels. The osteogenic fibres are covered with osteoblasts, and as the bone forms, some of these become left as bone-corpuscles within lacunæ. Thus in every particular the development of these bones resembles that of the subperiosteal layer of endochondral bone; which is, therefore, also to be considered as an instance of intramembranous ossification, although taking place on the surface of cartilage. Moreover, it is the same subperiosteal tissue which, in endochondral ossification, deposits the true or secondary bone upon those parts of the calcified cartilage-matrix which have escaped absorption; and this must also, therefore, be reckoned as developed according to the same type. In fact, even in intracartilaginous ossification, very little of the calcified cartilage-matrix eventually remains; this being almost wholly absorbed and either replaced by true or fibrous bone which has been formed by osteblasts, or swept away to form the medullary and other cavities.

With reference to the origin of the osteoblasts, it has been thought by some authors that they are derived from the blood-vessels, and are in fact leucocytes which have wandered out of the vessels and have taken on the special osteogenic function. Another and a more probable view regards them as modified connective-tissue cells formed within the periosteum and merely accompanying the vessels into the interior of the ossifying cartilage. They have also been thought, but with less probability, to be formed by division and alteration of the cartilage-cells.

LESSON XIV.

STRUCTURE OF STRIATED MUSCLE.

1. Take a shred of muscle from a recently killed mammal, and on a dry slide carefully separate long pieces of muscular fibres (single fibres if possible) and stretch them out, keeping them moist during the process by breathing on the slide. Put a drop of serum or Ringer's solution on the cover-glass before placing this over the preparation. Study first with a low, then with a high power. Sketch all the appearances to be seen in a small piece of a fibre, focussing carefully the most superficial layers. Notice the oval nuclei immediately under the sarcolemma. Then allow a little dilute acetic acid to run under the cover-glass and watch its effect.

2. Prepare some fibres of frog's muscle in the same way, but mount in salt solution instead of serum. Notice the muscular substance shrinking away here and there from the sarcolemma, which then becomes distinctly visible. Sketch a piece of sarcolemma bridging across an interval thus produced.

3. Study transverse sections of muscle which has been hardened in alcohol or formol and stained. Mount in dammar varnish or xylol balsam. Examine the section of a fibre first with a low and then with a high power. Sketch the appearances which are seen.

In each of the above preparations measure the diameter of some of the fibres.

Sections of muscle-spindles may be searched for in the transverse sections of muscle.

4. Place in 1 per cent. osmic acid a small shred of mammalian muscular tissue which has been stretched upon a cork. After 24 hours, when it will be deeply stained, wash it in water and with needles break the fibres up in glycerine as finely as possible. Cover and examine with a high power.

5. Cut off the head of a small garden beetle or wasp, and bisect the trunk with scissors so as to expose the interior. Notice two kinds of muscular tissue, the one belonging to the legs greyish in colour, the other attached to the wings yellowish. Preparations of both kinds of muscle are to be made in the same way as living mammalian muscle (§ 1), but it is better to mount them in a drop of white of egg. In both preparations the dark-looking air-tubes or tracheæ form prominent objects ramifying amongst the fibres. Observe the structure of the two kinds of muscle so far as it can be made out in the fresh preparation. If the preparation is made quickly, waves of contraction will probably be observed passing along the fibres.

6. Make another preparation of the leg-muscles, mounting the muscle in vinegar. (Alcohol-hardened muscle of insect or crab may be used for this purpose.) Notice that the muscular substance swells up somewhat and becomes clearer, whilst the sarcoplasm-network, with its lines and dots, comes more distinctly into view. In a well-teased preparation of alcohol-hardened muscle, the fibres will be frequently found breaking across into disks. Make careful drawings from this preparation.

7. Rollett's method. Cut off the head of an insect (wasp, small beetle), bisect the trunk and place in 90 per cent. alcohol for from 24 to 48 hours

or more. Then take a small piece of each kind of muscle, and place in strong glycerine for some hours. Wash thoroughly with water and transfer to 1 per cent. chloride of gold solution: leave the pieces of muscle in this from 15 to 30 minutes according to their size. From the gold solution they are transferred to formic acid (1 part of the strong acid to 3 of water), and kept in the dark for 24 hours, but they may be kept longer without disadvantage. The muscle is then teased in glycerine. Some of the fibres will be found after this method to have their sarcoplasm darkly stained, and to show, therefore, the appearance of a network both in longitudinal and transverse view: others, on the other hand, have the sarcous elements of the fibrils or sarcostyles stained, whilst the sarcoplasm has remained colourless.

Voluntary muscle is composed of long cylindrical fibres, measuring on an average about 0·05 mm. in diameter ($\frac{1}{500}$ inch) in mammalian muscles, and often having a length of an inch or more. Each fibre has an elastic sheath, the *sarcolemma*, which encloses the contractile substance. The sarcolemma is seldom visible, unless the contained substance becomes broken (fig. 151).

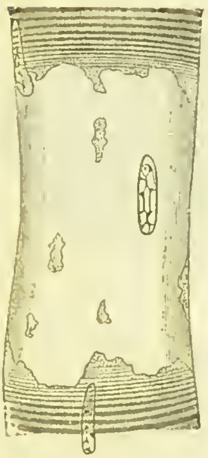


Fig. 151.

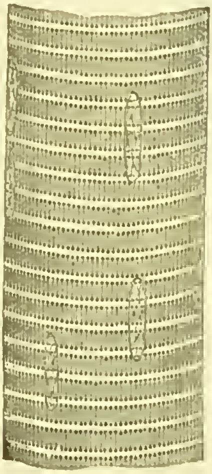


Fig. 152.

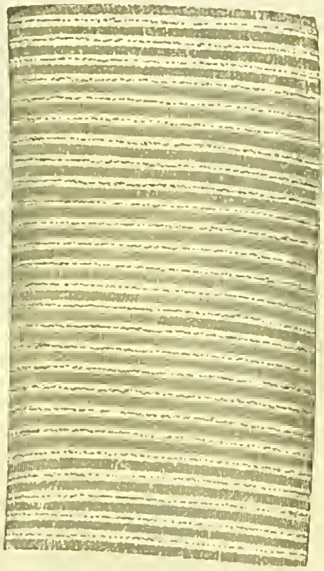


Fig. 153.

Fig. 151.—Sarcolemma of mammalian muscle highly magnified.
The fibre is represented at a place where the muscular substance has become ruptured and has shrunk away, leaving the sarcolemma (with a nucleus adhering to it) clear. The fibre has been treated with serum acidulated with acetic acid.

Fig. 152.—Muscular fibre of a mammal examined fresh in serum, highly magnified, the surface of the fibre being accurately focussed.
The nuclei are seen on the flat at the surface of the fibre, and in profile towards the edge.

Fig. 153. Portion of a medium-sized human muscular fibre, showing the intermediate line (Dobie's line) mentioned in the text. (Sharpey.)

The contractile substance of the fibre is characterised by the alternate dark and light stripes which run across the length of the fibre: hence the name *cross-striated* or *striped muscle.* On focussing, it can be seen that the stripes pass through the whole thickness of the fibre; they may therefore be looked upon as representing alternate disks of dark and light substance. If the fibre be very carefully focussed, rows of apparent granules are seen lying in or at the boundaries of the light streaks, and very fine longitudinal lines may, with a good microscope, be detected uniting the apparent granules. These fine lines, with their enlargements, the granules, are more conspicuous in the muscles of insects. They indicate the divisions between the longitudinal elements (*fibrils* or *sarcostyles*) which compose the fibre, and in preparations treated with dilute acid the lines appear to form part of a fine network, which pervades the muscle substance, and serves to unite the granules both transversely and longitudinally. This network, which is sometimes very distinct in preparations of muscle treated with chloride of gold, is, however, a network in appearance only: in reality it is the optical expression of the interstitial substance which lies between the fibrils. This substance is termed *sarcoplasm.*

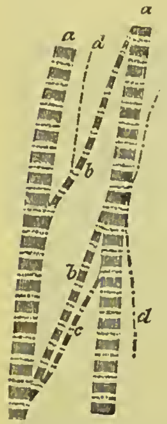


FIG. 154.

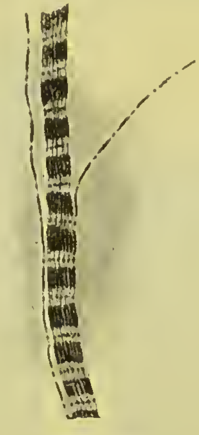


FIG. 155.

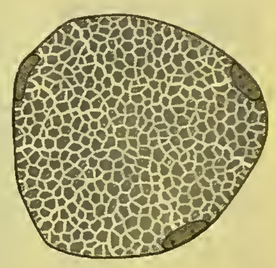


FIG. 156.

FIG. 154.—SMALL PORTION OF A HUMAN MUSCULAR FIBRE TEASED INTO SMALL LONGITUDINAL FRAGMENTS. (Sharpey.) Magnified about 800 diameters. *a*, *b*, *c*, larger and smaller groups of fibrils; *d*, ultimate fibrils.

FIG. 155.—SMALL PORTION OF A MUSCLE FIBRE OF CRAB SPLITTING UP INTO FIBRILS. (From a photograph.) Magnified 600 diameters.

FIG. 156.—SECTION OF A MUSCULAR FIBRE, SHOWING AREAS OF COHNHEIM. Three nuclei are seen lying close to the sarcolemma.

On examining the transverse section of a fibre with a high power, it is seen to be subdivided everywhere into small angular fields, *Cohnheim's areas* (fig. 156), which are themselves again divided up into minute dot-like areas. The smallest divisions represent sections of the fibrils of which the fibres are composed, and into which they may be split after death, especially after being hardened in certain reagents, *e.g.* chromic acid or osmic acid. The larger areas represent groups of fibrils. These areas of Cohnheim are usually polyhedral, but they may be elongated, and disposed either radially or concentrically with the circumference of the section. The interstitial substance or sarcoplasm lies between the fibrils and can be made visible by treatment with dilute acid or by staining with chloride of gold (figs. 158, 159, and 160). It is sometimes in relatively large amount, but in most muscular fibres is reduced to a very fine interstitium.

An ill-defined clear line is sometimes seen running transversely across the fibre in the middle of each dark band. This is termed *Hensen's line.*

If instead of focussing the surface of the fibre it be observed in its depth, an appearance different from that shown in fig. 152 is frequently visible, namely, a fine dotted line (*Dobie's line*), bisecting each clear stripe (fig. 153); this appearance is often considered to represent a membrane (*Krause's membrane*), which subdivides the fibrils at regular intervals (see p. 134). But the membranes of the individual fibrils or sarcostyles are rarely, if ever, visible in an intact mammalian fibre, and it is certain that the appearance of such a line in the middle of the clear stripe of an intact fibre is in most cases due to interference, caused by the light being transmitted between disks of different refrangibility.

Haycraft has suggested that the cross-striation of voluntary muscle is due to refractive effects produced by a varicosity of the component fibrils, basing his view upon the fact that in impressions of the fibres made in soft collodion all the cross-striation which are observed in the fibre itself are reproduced. There is no doubt that a well-marked cross-striated appearance can be produced in homogeneous fibrils by regularly-occurring varicosities, and many of the appearances observed in muscle may, as Haycraft contends, be referred to this cause. But even when a fibre or fibril is stretched so that it exhibits no varicosities, the cross-striations are still perfectly distinct. Moreover, in view of the entirely different manner in which the substance of the dark and clear stripes behave to many staining reagents, and especially to chloride of gold when applied as directed in § 7, the fact being that very definite structural appearances can under these circumstances be made out, the homogeneity of the muscle-fibril cannot be admitted. This inference is strongly confirmed by the microchemical work of A. B. Macallum, who has shown that the potassium salts of the wing muscle-fibrils are accumulated in a portion only of the fibril (fig. 165).

Nuclei.—Besides the sarcolemma and striated substance, a muscular fibre also exhibits a number of oval nuclei which have the usual structure of cell-nuclei : their chromatin often has a spiral arrangement. Sometimes there is a little granular substance (protoplasm) at each pole of the nucleus; each nucleus with the adjacent protoplasm has then been spoken of as a *muscle-corpuscle.* But the protoplasm which is adjacent to the nuclei is in all probability continuous with the sarcoplasm between the fibrils; both being the remains of the original

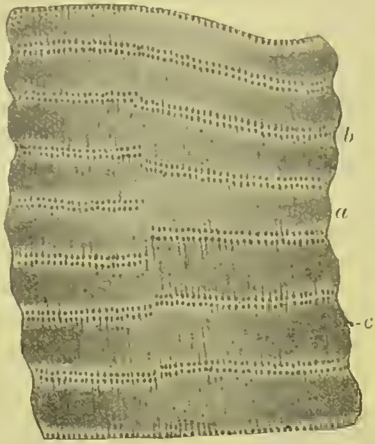


FIG. 157.—LIVING MUSCLE OF WATER-BEETLE (DYTISCUS MARGINALIS). Highly magnified.

a, dim stripe; *b*, bright stripe; *c*, fine lines with dot-like enlargements upon them which represent the interfibrillar sarcoplasm.

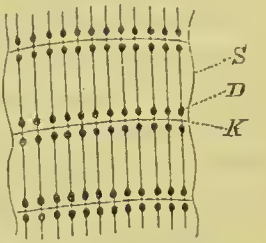


FIG. 158.—PORTION OF LEG-MUSCLE OF INSECT TREATED WITH DILUTE ACID.

S, sarcolemma; *D*, dot-like enlargement of sarcoplasm; *K*, Krause's membrane. The sarcous elements are dissolved or at least rendered invisible by the acid.

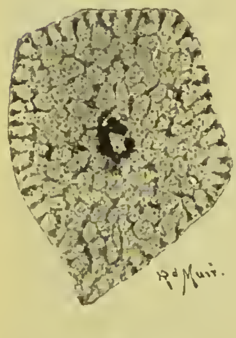
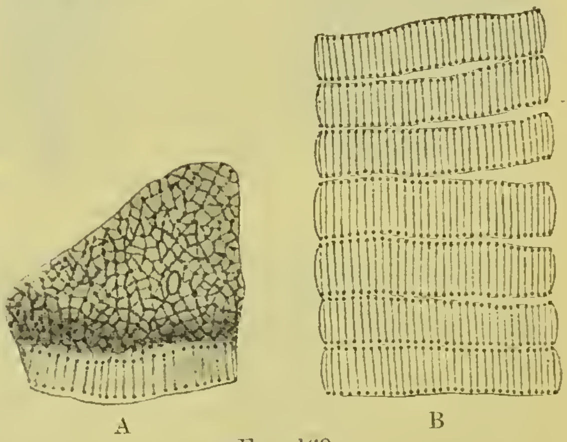


FIG. 159.



A

B

FIG. 160.

FIG. 159.—TRANSVERSE SECTION OF LEG-MUSCLE FIBRE OF AN INSECT, STAINED WITH GOLD CHLORIDE.

The sarcoplasm is here stained, and appears in the form of a network, in the meshes of which lie the sections of the fibrils. Notice the mottled appearance of the sections of the sarcostyles or fibrils, indicating a porous structure, as in the wing fibrils (see fig. 163). The central protoplasm (with a nucleus) is also evident. (From a photograph.)

FIG. 160.—LEG-MUSCLE FIBRE OF INSECT TREATED WITH DILUTE ACID, SHOWING A TENDENCY TO BREAK ACROSS INTO DISKS.

The sarcoplasm is in the form of fine lines. The ordinary dark stripes of the fibre have disappeared in the acid. A, a disk seen partly in section and exhibiting the reticular arrangement of the sarcoplasm; B, longitudinal view of fibre.

undifferentiated protoplasm of the cells from which the muscular fibres are developed. In the mammalian muscle the nuclei usually lie immediately under the sarcolemma (figs. 151, 152, 156), in frog's muscle they are scattered throughout the substance of the fibre. Some animals, such as the rabbit, have, besides muscles of the ordinary type of structure, which in this animal are pale in colour, others of a deep red colour. These *red muscles* were found by Ranvier to exhibit certain differences both in structure and function. One difference of structure is that the nuclei, which are numerous, are not confined to the surface, but are scattered throughout the substance of the fibres. The fibres in question also contain more sarcoplasm than the ordinary fibres, and their blood-vessels have a peculiarity of structure which will be afterwards noticed. Here and there, in all mammals, amongst the ordinary fibres are some in which the nuclei are distributed through the thickness of the fibres; this is the case also, as just remarked, with all the muscular fibres of the frog. In muscles which are in constant activity, such as the diaphragm and the dorsal fin muscles of Hippocampus, the protoplasm (sarcoplasm) of the fibres is present in relatively large proportion, and this is also the case with the wing muscles of insects.

The transverse section of a muscle shows the fibres to be nearly cylindrical in figure. Between the fibres there is a certain amount of areolar tissue, which serves to support the blood-vessels and also unites the fibres into fasciculi; the fasciculi are again united together by a larger amount of this intramuscular connective tissue (*endomysium*).

Ordinary or leg-muscles of insects.—In the muscles of insects the stripes are relatively broad, and their structure can be more readily seen than in mammals. In the living fibres from the muscles which move the legs, the sarcoplasm presents a striking appearance of fine longitudinal lines traversing the muscle, and enlarging within the light stripes into rows of dots (figs. 157, 161). This is still better seen in fibres and portions of fibres which have been treated with dilute acid (figs. 158, 160). In separated disks produced by the breaking across of muscle-fibres, the surfaces of the disks show a network with polyhedral meshes in some insects (fig. 160, A), one formed of lines radiating from the centre of the fibre in others. The nuclei, with some inclosing protoplasm, lie in the middle of the fibre (fig. 159).

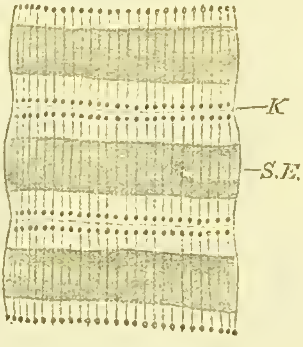


FIG. 161.—LEG-MUSCLE FIBRE OF INSECT, STAINED WITH GOLD CHLORIDE BY ROLLETT'S METHOD. *K*, line formed by membranes of Krause; *S.E.*, dark stripe formed by sarcous elements. The sarcoplasm has the appearance of longitudinal lines.

Wing-muscles of insects.—The wing-muscles of insects are easily broken up into fibrils (sarcostyles), which also show alternate dark and light striæ (fig. 162).

The sarcostyles are subdivided at regular intervals by thin transverse disks (*membranes of Krause*) into successive portions, which are termed *sarcomeres*. Each sarcomere is occupied by a portion of the dark stria of the whole fibre (*sarcous element*): the sarcous element is really double, and in the stretched fibril separates into two at the line of Hensen (fig. 162, B). At either end of the sarcous element is a clear substance (probably fluid or semi-fluid) separating it from the membrane of Krause: this clear substance is more evident the more the fibril is extended, but diminishes, even to complete disappearance, in the contracted muscle (fig. 162, A). The cause of this change is explained when we study more minutely the structure of the sarcous element. For we find that each sarcous element is pervaded with longitudinal canals or pores, which are open in the direction of Krause's

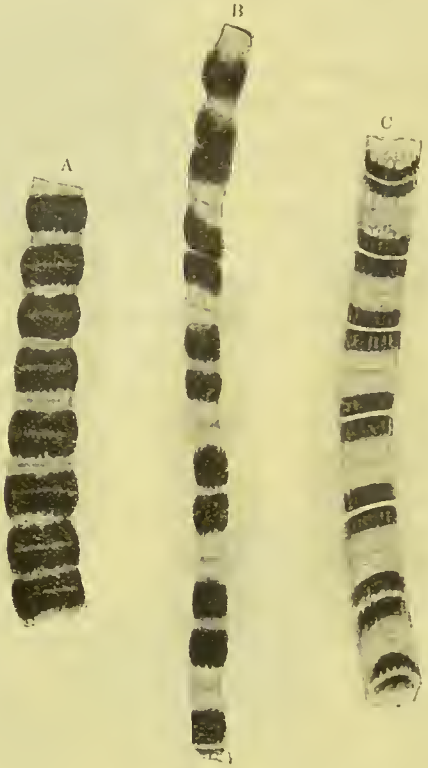


FIG. 162.—FIBRILS OF THE WING-MUSCLES OF A WASP, PREPARED BY ROLLETT'S METHOD. Highly magnified.

A, a contracted fibril. B, a stretched fibril, with its sarcous elements separated at the line of Hensen. C, an uncontracted fibril, showing the porous structure of the sarcous elements.

membranes, but closed at the middle of the sarcous element (figs. 163, 164). In the contracted muscle, the clear part of the muscle-substance has nearly disappeared from view, but the sarcous element is swollen and the sarcomere is thus shortened : in the uncontracted muscle, on the other hand, the clear part occupies a considerable interval between the sarcous element and the membrane of Krause, the sarcomere being lengthened and narrowed. This difference is well seen with certain methods of staining. The sarcous element does not lie free in the middle of the sarcomere, but is attached at either end to Krause's membrane by very fine lines, which may represent fine septa, running through the clear substance (fig. 164); on the other hand, Krause's membrane appears to be attached laterally to a fine membrane which limits the fibril externally.

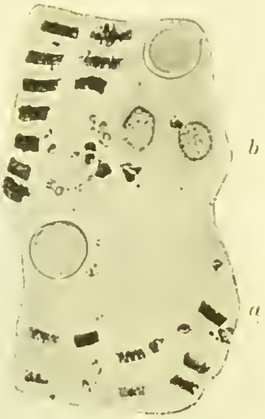


FIG. 163.—ISOLATED SARCOUS ELEMENTS OF A WING-MUSCLE, SHOWING THE TUBULAR OR POROUS STRUCTURE. Untouched photograph. Magnified 870 diameters.

At *a* some are seen in profile; at *b* on the flat. The two circular bodies are fat-drops.

The planes of sarcous elements set side by side in a muscle-fibre form the dark stripe (the so-called *principal disk*) of the muscle-substance of ordinary muscle-fibres (fig. 161). In the wing-muscles of insects the fibrils are surrounded by granular sarcoplasm, and the whole fibre is therefore very indistinctly cross-striated, although each individual fibril is markedly so (fig. 162). As already stated, the sarcous elements are remarkable for containing a large proportion of potassium salts (fig. 165).

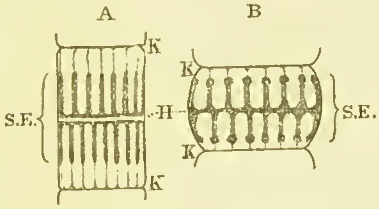


FIG. 164.—DIAGRAM OF A SARCOMERE IN A MODERATELY EXTENDED CONDITION, A, AND IN A CONTRACTED CONDITION, B.

K, K, membranes of Krause; H, line or plane of Hensen; S.E., poriferous sarcous element.

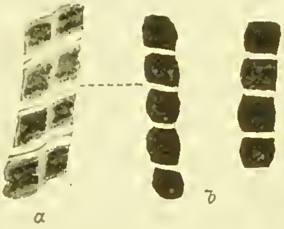


FIG. 165.—LOCALISATION OF POTASSIUM IN SARCOUS ELEMENTS OF WING-MUSCLE OF BEETLE. (A. B. Macallum.)

a, resting; *b*, contracted.

Sometimes in the ordinary (leg) muscles of arthropods what look like detached dot-like portions of the sarcous element are seen within the clear stripes, lying usually near Krause's membrane. The rows of such dots have been termed *accessory disks*. Most muscles show no accessory disks, but the sarcoplasmic enlargements between the fibrils (fig. 158, D) are often mistaken for them.

Muscle in polarised light.—When muscle fibres are examined with polarised light between crossed nicols, the sarcous elements (which form the dark stripe) are seen to be doubly refracting (anisotropous), while the clear substance (forming the light stripe) is singly refracting (isotropous). In contracted parts of the muscle the (anisotropous) sarcous elements are seen to have increased in bulk, while the isotropous substance of the clear stripe has correspondingly diminished in amount (fig. 166, B).

Merkel described a reversal of the stripes during contraction, *i.e.* a transference of the anisotropous substance of the dark stripe from Hensen's line to Krause's membrane, the place of the dark stripes thus becoming occupied by clear material, that of the light stripes by dark. He further described this condition as being preceded by an intermediate stage in which the fibril shows homogeneity of shading. No doubt in the ordinary muscle-fibres of arthropods, when we observe the so-called 'fixed' waves of contraction, there is an apparent blurring of the cross-striation of the fibre just where the muscle is passing from extension to contraction, but this appearance is explicable by the unequal pull of the contracted parts of the fibrils upon those which are not yet contracted. The contraction in each fibre starts from the nerve-ending, which is at one side of the fibre, and spreads

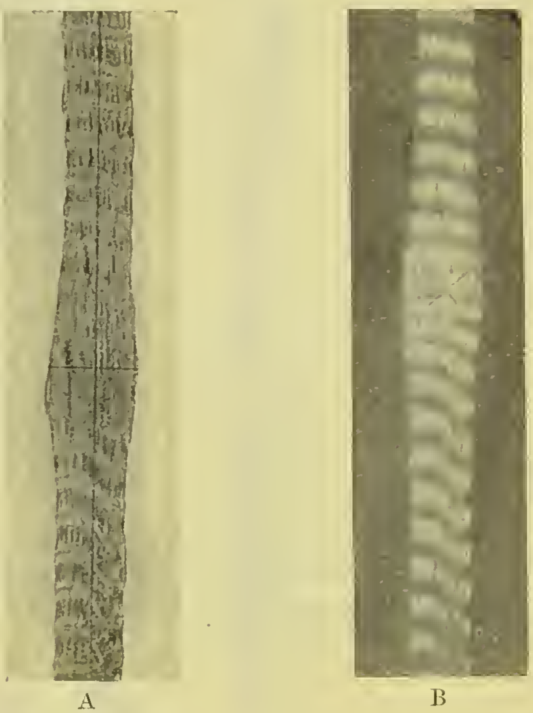


FIG. 166.—LEG-MUSCLE FIBRE OF CHRYSOMELA CŒRULEA WITH (FIXED) CONTRACTION WAVE PHOTOGRAPHED UNDER POLARISING MICROSCOPE.[1]

A, with uncrossed nicols; B, with crossed nicols.

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[1] I am indebted to the late Professor Engelmann for these two photographs.

first across the fibre and then tends to pass as a wave towards either end. But the one side always has a start in the progress of this wave, and the fibrils must thus receive an unequal pull, so that they are shifted along one another and the line of cross-striping is broken up. That no transference of anisotropous substance really occurs is at once clear from the appearance of the contracting fibre under polarised light (fig. 166, B), and the study of the isolated fibrils of wing-muscle gives no support to the theory of reversal, although it is widely held by German authors. That the apparent reversal is not real is also illustrated by fig. 167, which represents a leg muscle fibre of an insect in process of contraction. The dark bands of the contraction-wave are seen to be really due to accumulations of sarcoplasm. These accumulations appear as dark lines which obscure the continuity of the fibrils, and by contrast cause the whole of the sarcomeres between them to appear light.

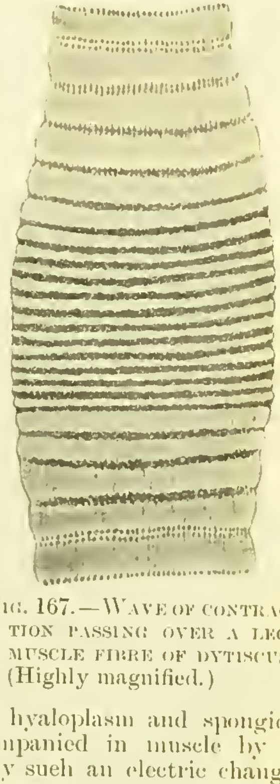

FIG. 167.—WAVE OF CONTRACTION PASSING OVER A LEG-MUSCLE FIBRE OF DYTISCUS. (Highly magnified.)

Mechanism of contraction.—Comparing the structure of the sarcomere with that of protoplasm we find in both a framework (spongioplasm, substance of sarcous element) which incloses in its meshes or pores a clear, probably fluid substance (hyaloplasm, clear substance of sarcomere), (although the differentiation into spongioplasm and hyaloplasm is not evident in all protoplasm). In both also the clear substance or hyaloplasm, when the tissue is subjected to stimulation, passes into the pores of the porous substance or spongioplasm (contraction), whilst in the absence of such stimulation it tends to pass out from the spongioplasm (formation of pseudopodia, resting condition of muscle). The effect of stimulation appears in both structures to be the production of a change in surface tension (perhaps between the hyaloplasm and spongioplasm); this change being demonstrably accompanied in muscle by a difference in electric potential. In all probability such an electric change occurs in all protoplasm. Thus both the movements of cell-protoplasm and those of muscle are in all probability brought about by like means, although at first sight the structure of muscle is dissimilar from that of protoplasm. We have already noticed that the movements of cilia are susceptible of a somewhat similar explanation.

Macdonald has suggested that the movements of fluid from one part of the sarcomere to the other is a result of osmosis, caused by the sudden setting free of electrolytes (potassium salts) in the substance of the sarcous element just previous to the actual contraction.[1]

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[1] See his article on this subject in the *Quart. Journ. Exper. Physiol.*, vol. ii. 1909, p. 5. MacDougall had previously suggested that such osmosis might occur between the interior of the fibril and the sarcoplasm outside. But there are many reasons against this hypothesis, a criticism of which will be found in the *Quart. Journ. Exper. Physiol.*, vol. iii. 1910, p. 63. It is in any case extremely improbable that such rapid changes as occur in the contraction of muscle, would be the result of osmotic movements.

LESSON XV.

CONNECTION OF MUSCLE WITH TENDON; BLOOD-VESSELS OF MUSCLE; CARDIAC MUSCULAR TISSUE; DEVELOPMENT OF MUSCLE; PLAIN MUSCULAR TISSUE.

1. To study the connection of muscle with tendon, a frog is killed by destruction of the brain and spinal cord, and placed in about a litre of water raised to a temperature of 55° C. It is left in this for 15 minutes, the water gradually cooling. It is then easy to dissociate the muscular fibres in large numbers. To observe their attachment to the tendon-bundles a fine longitudinal shred must be snipped off with scissors at the tendinous attachment, and dissociated upon a slide in a drop of water. It will usually be found that the muscular substance is retracted from the end of the sarcolemma tube, which is firmly cemented to the tendon-bundle. The structure may be brought more distinctly into view by adding to the dissociated fibres a drop of a weak solution of iodine in salt solution or in serum (iodised serum).[1]

2. The blood-vessels of muscle. These are studied in longitudinal and transverse sections or in flattened-out pieces of injected muscle. It will be noticed that the capillaries are very numerous, and form a network with oblong meshes. In the red muscles of the rabbit, small dilatations are seen on the transverse cords of the network.

3. The muscular tissue of the heart is studied in sections of that organ (see Lesson XXVII.) and also in teased preparations. To prepare the latter, place a small piece of heart-muscle in 33 per cent. alcohol for a few days; stain in picro-carmine solution for some hours or days; and tease in dilute glycerine.

4. Tear off a small shred of the circular muscular coat of a piece of dog's or cat's intestine which has been for 48 hours or more in $\frac{1}{8}$ per cent. bichromate of potash solution or in 33 per cent. alcohol. Hold the shred with forceps in a drop of water on the slide and fray it out with a needle. In this process many cells will be set free and can be found with a low power. The preparation may then be covered and examined with a high power. Sketch one of the cells. Then allow very dilute hæmatoxylin solution to pass under the cover-glass and lastly a drop of glycerine. Sketch another cell after staining. Measure two or three cells and their nuclei. Sections of involuntary muscle will be seen and can be studied along with the viscera which possess muscular coats.

Ending of muscle in tendon.—A small tendon-bundle passes to each muscular fibre and becomes firmly united with the sarcolemma which extends over the end of the fibre (fig. 168). Besides this immediate attachment, a further connection is established by the fact that the areolar tissue between the tendon-bundles is continuous with that which lies between the muscular fibres.

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[1] This method is the one given by Ranvier (*Traité Technique*, p. 395). The muscle-endings may also sometimes be well seen at the extremities of the tendons which are removed from the mouse's tail in the manner described in Lesson X.

Blood-vessels of muscle.—The capillaries of muscular tissue are very numerous. They run, for the most part, longitudinally, with transverse branches, so as to form long oblong meshes (fig. 169). No blood-vessels ever penetrate the sarcolemma. In the red muscles of the rabbit, the transverse capillaries have small dilatations upon them (fig. 170). Associated with this and other peculiarities of structure (see p. 133), it is found that the red muscles have a much slower rate of contraction, and a much longer period of latency than the ordinary muscles.

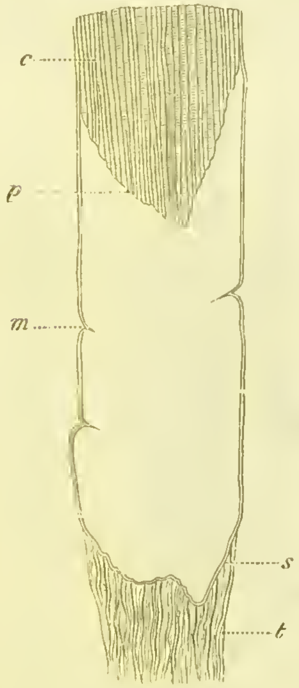

FIG. 168.—TERMINATION OF A MUSCULAR FIBRE IN TENDON. (Ranvier.)

m, sarcolemma; *s*, the same membrane passing over the end of the fibre; *p*, extremity of muscular substance; *c*, retracted from the lower end of the sarcolemma-tube; *t*, a tendon-bundle passing to be fixed to the sarcolemma.

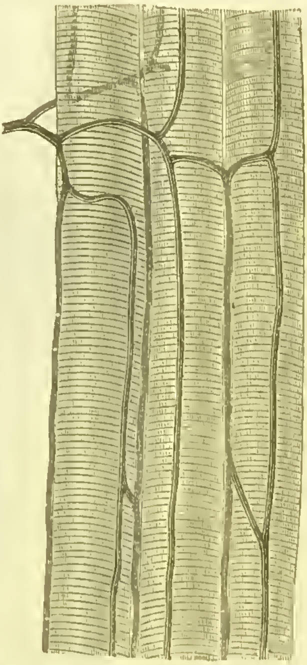

FIG. 169.—CAPILLARY VESSELS OF MUSCLE.

Lymph-vessels, although present in the connective-tissue sheath (perimysium) of a muscle, do not penetrate between the component fibres.

The **motor nerves** of voluntary muscles pierce the sarcolemma and terminate in ramified expansions known as *end-plates* or *motor end-organs*; the *sensory nerves* end in groups of specially modified muscle fibres known as *muscle spindles* (see Lesson XIX.).

Development.—Voluntary muscular fibres are developed from embryonic cells of the mesoderm (muscle-plate), which become elongated, and the nuclei of which become multiplied, so as to produce long slender, multi-nucleated fusiform or cylindrical embryonic fibres. It is not quite clear whether, as has usually been supposed, the whole fibre is thus formed of a single enlarged cell, or whether it may be produced by the joining together end to end of a number of cells of the muscle-plate (or even of more than one muscle-plate), so as to produce a syncytium, within which the striated fibrils make their appearance. These appear at first along one side of the fibre, the change gradually extending around the circumference and also penetrating towards the centre; but the protoplasm at the middle of the fibre, to which the nuclei are presently confined, and at the side opposite to that at which the differentiation began, remains for some time unaltered in character (fig. 171). Eventually the change in structure extends to these parts also, and the nuclei pass gradually to occupy their ordinary position under the sarcolemma, which has by this time become formed. The

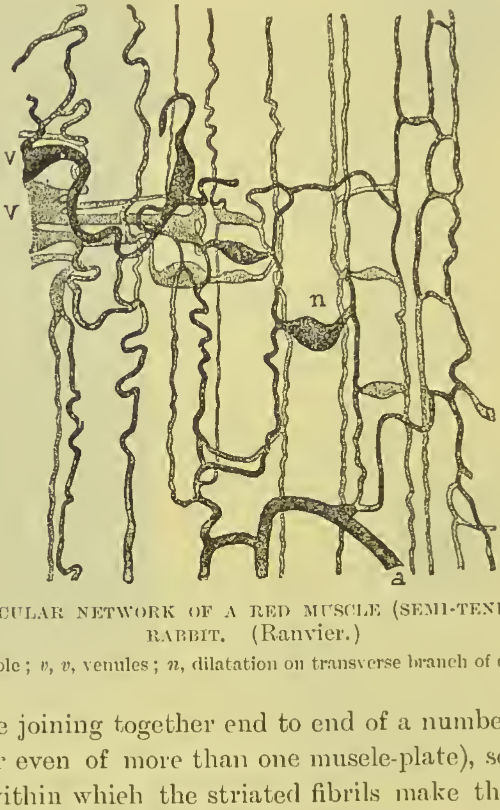

FIG. 170.—VASCULAR NETWORK OF A RED MUSCLE (SEMI-TENDINOSUS) OF THE RABBIT. (Ranvier.)

a, arteriole; *v*, *v*, venules; *n*, dilatation on transverse branch of capillaries.

sarcolemma is believed to be produced, not by the muscle-fibre itself, but by the mesenchyme or connective-tissue cells between the fibres, since it is directly continuous with the connective-tissue bundles of the tendon and of the interstitial tissue.

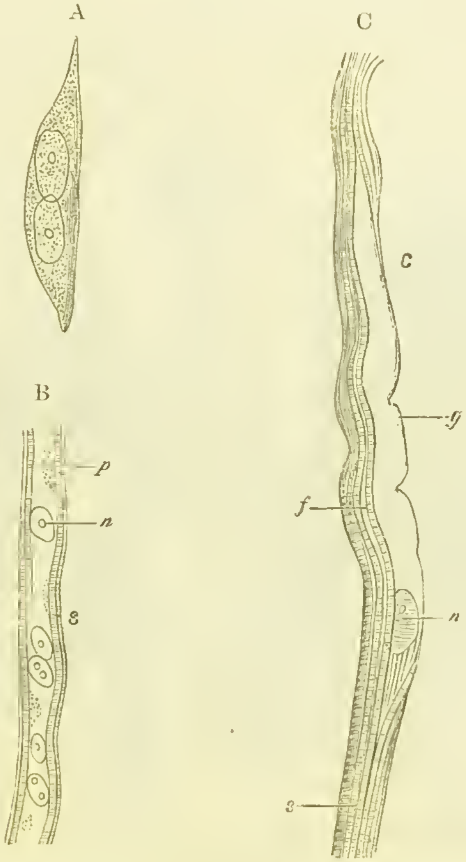

Fig. 171.—Developing muscular fibres.

A, elongated cell with two nuclei. A striation is beginning in the protoplasm along one side of the cell; from fœtal sheep. (Wilson Fox.)

B, from human fœtus of two months. (Ranvier.) *p*, central protoplasm with several nuclei, *n*, scattered in it; *s*, commencing sarcolemma, with striated muscular substance developing immediately beneath it.

C, from human fœtus of three months. (Ranvier.) The contractile substance, *s*, *f*, now almost incloses the unaltered protoplasm, *g*; only one nucleus, *n*, is represented.

CARDIAC MUSCLE.

The muscular substance of the heart is composed of transversely striated muscular fibres, which differ from those of voluntary muscle in the following particulars, viz.:—their striations are less distinct; they have no sarcolemma, although there is a thin superficial layer of non-fibrillated substance; they branch and unite by their branches and also at the side with neighbouring fibres, and their nuclei lie in the substance and often near the centre of the fibres. In man and many mammals the fibres are marked off into a series of short cylindrical cells (figs. 172, 173) joined together end to end and side to side, each corresponding to one of the nuclei. The junctions of these cells may be seen in longitudinal sections appropriately stained; they come also distinctly into view in sections of the fresh tissue stained with nitrate of silver. They appear to be bridged across by fine fibrils, continued into the cells above and below the lines of junction (figs. 174, 175). These lines have usually been regarded as intercellular spaces separating the constituent cells of the tissue from one another (Schweigger-Seidel). Some authorities (Przewosky, v. Ebner, M. Heidenhain) are inclined to regard the cardiac muscular tissue as forming a syncytium, the cells being all continuous both laterally and longitudinally, and the apparent intercellular lines being special differentiations. These, according to v. Ebner, are due to localised contractions, but, according to Heidenhain, represent portions of the fibres at which growth in length occurs (analogous to the suture-lines between the flat bones of the cranium). As against this view of the structure of the heart-muscle, and in favour of that of Schweigger-Seidel, must be set the silver-staining of the supposed cell-junctions, and the fact that it is easily possible in some animals to separate the

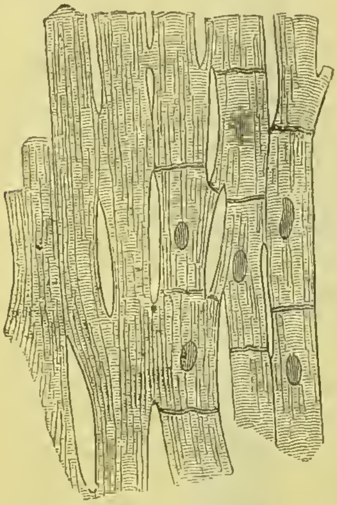

Fig. 172.—Muscular fibres from the heart, magnified, showing their cross-striæ, divisions, and junctions. (Schweigger-Seidel.)

The nuclei and cell-junctions are only represented on the right-hand side of the figure.

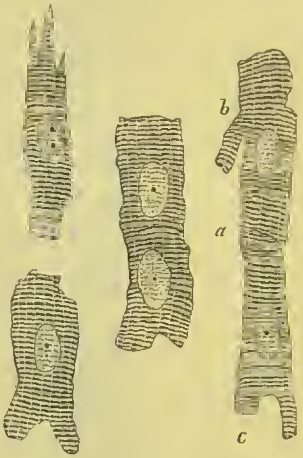

Fig. 173.—Six muscular fibre-cells from the heart. Magnified 425 diameters.

a, line of junction between two cells; *b*, *c*, branching of cells. (From a drawing by J. E. Neale.)

fibres after maceration into short uninucleated fragments as in fig. 173. Schweigger-Seidel's view has been recently upheld by the observations of v. Palczewska and Werner, who have studied the subject in the heart of man and of various mammals. These observers point out, as had been previously done in the last edition of this work, that the short non-nucleated lengths of fibres (fig. 174), which Heidenhain regards as fatal to the cellular theory, may be parts of cells lying in other planes of the myocardium, which are inserted between those belonging to the plane included in the longitudinal section. On the other hand, the continuity of the muscular fibrils within the masses of Purkinje's fibres under the endocardium in the sheep, the fibrils around one cell being freely continued around the neighbouring cells (see fig. 361, p. 288), is in favour of the syncytial theory. Further, in many vertebrates, including some mammals, no cell-territories can be made out in the myocardium.

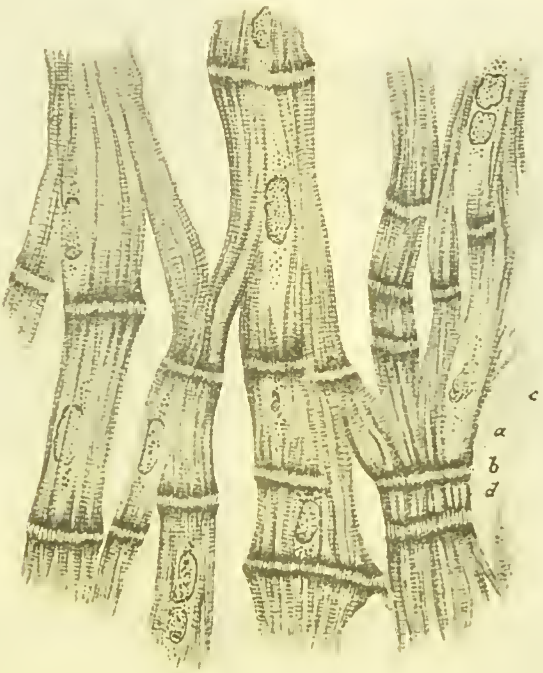

FIG. 174.—CARDIAC MUSCLE-FIBRES, SHOWING THEIR BRANCHING AND JUNCTIONS. (Przewosky.)

The intercellular junctions are very well marked. In some of the fibres, as at *a*, two junctional lines are close together with a non-nucleated portion, *d*, between them; *b*, fibrils passing across junction; *c*, a nucleus.

The explanation of these differences appears to lie in the fact that in all heart-muscle at a certain period of development (fig. 176) the cells form a syncytium within which the contractile fibrils are developed, and only in mammals is a differentiation of the syncytium into cells produced; the lines of junction being even here bridged across by the muscle-fibrils.

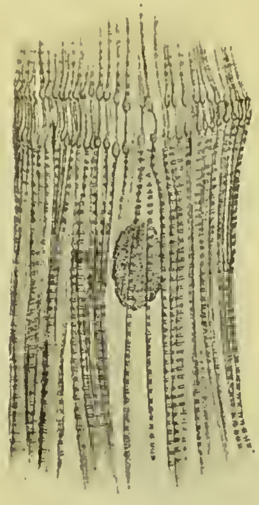

FIG. 175.—PORTION OF CARDIAC MUSCLE EXHIBITING CONTINUITY OF FIBRILS ACROSS JUNCTIONAL LINE. (Przewosky.) Highly magnified.

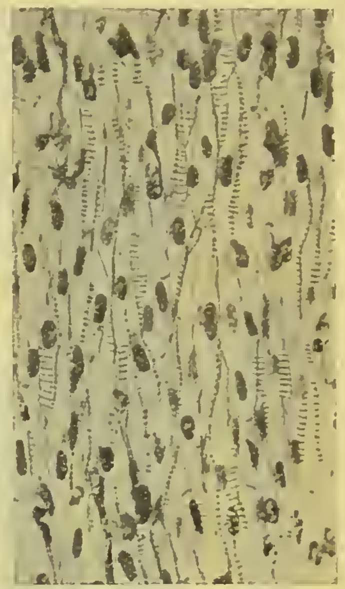

FIG. 176.—SECTION FROM HEART OF FIVE MONTHS' EMBRYO, HUMAN. (G. Mann.)

Although it is usually stated that there is no sarcolemma in cardiac muscle fibres, v. Palczewska and Werner describe and figure a membrane covering the cardiac cells which they regard as equivalent to the sarcolemma of voluntary muscle.

NON-STRIATED, SMOOTH OR PLAIN MUSCLE.

Involuntary or **plain muscular tissue** is composed of long, somewhat flattened, fusiform cells (figs. 177, 178), which vary much in length. Each cell has an oval or rod-shaped nucleus, which shows the usual intranuclear network and commonly one or two nucleoli. There is a centriole—sometimes double—close to the nucleus (fig. 179). The cell-substance is finely fibrillated, but does not exhibit cross-striæ like those of voluntary muscle. There appears, as in cardiac muscle, to be a delicate non-striated external layer, probably a stratum of undifferentiated protoplasm, but not a true sarcolemma. Next to this, in some smooth muscle, is a layer containing coarser fibrils (boundary fibrils of M. Heidenhain) (fig. 178). Frequently there are seen on involuntary fibres a series of somewhat irregularly placed transverse markings which appear as knot-like condensations of the cell-substance (figs. 178, 180) staining somewhat differently from the rest of the cell. The nature of these is not well understood, but they are perhaps fixed contraction waves (C. M‘Gill); the fibrils are enlarged as they run through the knots. There is a little intercellular substance which can be stained by nitrate of silver, and which is bridged across by filaments passing from cell to cell (fig. 181). Some authorities, however, deny that the involuntary cells are thus connected, and hold

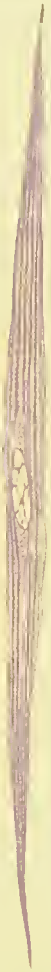

FIG. 177.

FIG. 178.

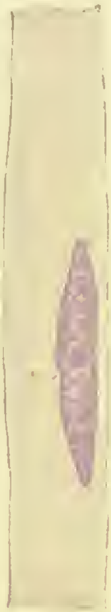

FIG. 179.

FIG. 177.—MUSCULAR FIBRE-CELL FROM THE MUSCULAR COAT OF THE SMALL INTESTINE, HIGHLY MAGNIFIED.

A complete cell, showing the nucleus with intra-nuclear network, and the longitudinal fibrillation of the cell-substance.

FIG. 178.—PORTION OF A PLAIN MUSCLE-CELL, SHOWING FIBRILS WITHIN ITS CYTOPLASM. Magnified 450 diameters.

FIG. 179.—PLAIN MUSCLE FIBRE, SHOWING NUCLEUS, CENTRIOLE, AND CYTOPLASM WITH FIBRILS. (Lenhossék.)

that the appearance of bridging fibres is due to intercellular connective tissue. It is however difficult to understand how the contractions are propagated from cell to cell if there is no sort of continuity between the cells.

Plain muscular tissue is found chiefly in the walls of hollow viscera; thus it forms the muscular coat of the stomach and intestines, and occurs abundantly in the muscular coat of the gullet, although it is here intermixed with cross-striated muscle; it is found also in the mucous membrane of the whole alimentary canal from the œsophagus downwards; in the trachea and its ramifications; in the urinary bladder and ureters; in the uterus and Fallopian tubes; in the prostate; the spleen and lymphatic glands; the muscle of Müller in the orbit, and in the ciliary muscle and iris. The walls of gland-ducts also contain it; and the middle coat of the arteries, veins, and lymphatics is largely composed of this tissue. It occurs in the skin, both in the secreting parts of the sweat glands, and in small bundles attached to the hair-follicles: in the scrotum it is found abundantly in the

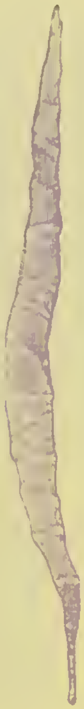

Fig. 180.—Fibre-cell from intestine, showing knot-like condensations of cell-substance. (Grützner.)

Fig. 181.—Muscle-cells of intestine. (Szymonowicz.) Magnified 530 diameters.

The fibres are represented in longitudinal section; and the interstices between them are seen to be bridged across by fine fibrils. *i*, interstice; *n*, nucleus.

subcutaneous tissue (dartos), and it also occurs in the areola of the nipple.

Development.—According to the observations of C. M'Gill, the smooth muscle of the alimentary canal (pig) is developed from the syncytium of mesenchyme cells which surrounds the entoderm. Some of these cells become elongated and spindle-shaped while retaining their inter-connection. Myofibrils are developed in their protoplasm. These are not confined to the limits of a single cell, but extend over two or even a large number of cells. The myofibrils are of two kinds, coarse and fine, varying in relative number in different parts. According to M'Gill, the inter-connection of the cells is seen even in the fully formed muscle, which retains its syncytial character, its cells being incompletely separated.

In certain situations smooth muscle is formed from epithelium, as with the muscular tissue of the sweat glands (Ranvier) and that of the iris (Nussbaum, Szili).

LESSON XVI.

STRUCTURE OF NERVE-FIBRES.

1. Tease a piece of fresh nerve rapidly in salt solution (or by the method of semidesiccation, keeping the preparation moist by the breath, afterwards mounting in salt solution). Touch the fibres as little and obtain them as long and straight as possible. Study the medullated fibres, carefully noticing all the structures that are visible—viz., nodes of Ranvier, nucleus of neurolemma, double contour of medullary sheath, medullary segments, etc. Measure the diameter of six fibres. Draw a short length of a fibre very exactly.

2. Prepare a piece of sympathetic nerve in the same way. The nerves passing to the spleen are well adapted for the study of non-medullated fibres. They are also found amongst the medullated fibres of the ordinary nerves. The nuclei may be stained by gentian violet.

3. Separate (in dilute glycerine) into its fibres a small piece of nerve (or nerve-root) that has been twenty-four hours in 1 per cent. osmic acid. The nerve should have been moderately stretched on a piece of cork by means of glass pins before being placed in the acid. Keep the fibres as straight as possible and only touch them near their ends with the needles. Sketch two portions of a fibre under a high power, one showing the node of Ranvier and the other a nucleus of the primitive sheath. Look for pale fibres. Measure the length of a nerve segment between two nodes of Ranvier.

4. Mount in xylol balsam or dammar sections of a nerve which has been hardened in picric acid and alcohol, or fixed with osmic acid and hardened in alcohol. The sections may be stained with picro-carmine or hæmatoxylin. The nerve should be pinned out straight upon a cork with glass pins before being placed in the hardening solution. Examine the sections first with a low and afterwards with a high power. Notice the lamellar structure of the perineurium, the varying size of the nerve-fibres, the axis cylinder in the centre of each fibre, etc. Measure the diameter of six fibres. Sketch a small portion of the section.

5. Study sections of splenic nerve placed as soon as possible after death in Flemming's solution.

6. Teased preparations and longitudinal sections from nerves which have been cut nearer the spinal cord. The nerves should be prepared with osmic acid as in § 3. Notice the breaking up of the myelin of the medullary sheath, varying in degree according to the length of time the section has been made previously. In preparations from the central cut end of the nerve prepared by Cajal's reduced silver method[1] new fibres may be seen budding from the extremities of the fibres of the stump.

Nerve-fibres are of two kinds, *medullated* and *non-medullated*. The cerebro-spinal nerves and the white matter of the nerve-centres are composed of medullated fibres; the sympathetic nerves near their peripheral distribution are largely made up of non-medullated fibres.

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[1] See Appendix.

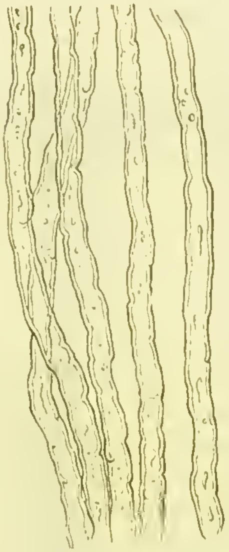

FIG. 182.—WHITE OR MEDULLATED NERVE-FIBRES, SHOWING THE SINUOUS OUTLINE AND DOUBLE CONTOURS. (Sharpey.)

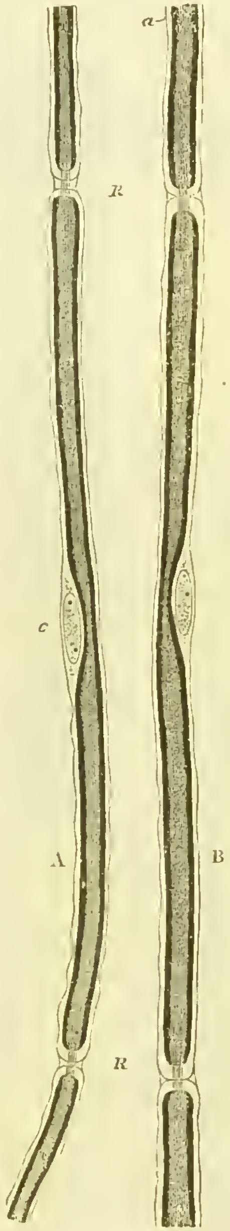

FIG. 183.—PORTIONS OF TWO NERVE-FIBRES STAINED WITH OSMIC ACID, FROM A YOUNG ANIMAL. Diagrammatic. (J. E. Neale.)

R, *R*, constrictions of Ranvier, with axis-cylinder passing through. *a*, neurolemma of the nerve; *c*, opposite the middle of the segment, indicates the nucleus and protoplasm lying between the neurolemma and the medullary sheath. In A the nodes are wider, and the intersegmental substance more apparent than in B.

FIG. 183.

The **medullated** or **white fibres** are characterised, as their name implies, by the presence of the so-called *medullary sheath* or *white* *substance.* This is a layer of soft substance, physically of a fatty nature, which encircles the essential part of a nerve fibre, viz., the *axis-cylinder.* Outside the medullary sheath is a delicate but tough homogeneous membrane, the *primitive sheath* or *nucleated sheath of Schwann*, but this is not present in all medullated fibres, being absent in those which are within the nerve-centres. The primitive sheath is known as the *neurolemma.*[1]

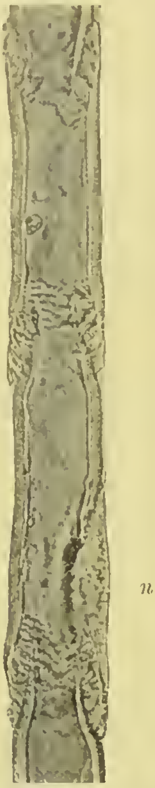

FIG. 184.—A SMALL PART OF A MEDULLATED FIBRE. Photograph. Magnified 600 diameters.

The fibre looks in optical section like a tube—hence the term tubular formerly applied to these fibres. Three partial breaches of continuity (medullary clefts) are seen in the medullary sheath, which at these places exhibits a tendency to split into laminæ. Elsewhere the medullary sheath shows coagulation-appearances. At n, is a nucleus belonging to the neurolemma, embedded in protoplasm, but the outline of the nucleus itself is not focussed.

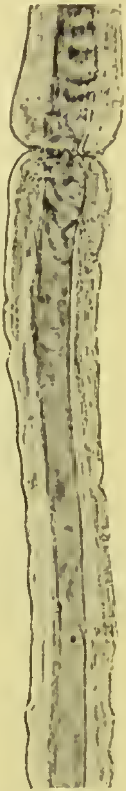

FIG. 185.—MEDULLATED NERVE-FIBRE, FRESH, SHOWING A NODE OF RANVIER. Photograph. Magnified 600 diameters.

The coagulation of the substance of the medullary sheath is advanced, and the axis-cylinder is slightly shrunken away from it, and is thus rendered distinctly visible.

The *medullary sheath* is composed of a highly refracting fatty material

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[1] Often termed "neurilemma," a name formerly applied to the sheath of Henle (see p. 156).

(myelin), which gives a characteristic dark contour and tubular appearance to the nerve-fibres (figs. 182, 184). It affords a continuous investment to the axis-cylinder, except that, as was shown by Ranvier, in the peripheral nerve-fibres it is interrupted at regular intervals. At these places the neurolemma appears to produce a constriction in the nerve-fibre, and the interruptions of the medullary sheath are accordingly known as the *constrictions* (Ranvier) or *nodes* (figs. 183, 186), the latter term being applied from the resemblance which they bear to the nodes of a bamboo. It is, however, uncertain whether the constriction is entirely occupied by the neurolemma itself or partly by a special band (*constricting band* of Ranvier) of a material which resembles intercellular substance in its reaction to nitrate of silver (fig. 196). The length of nerve between two successive nodes is termed an internode; in the middle of each internode is one of the nuclei of the neurolemma. Besides these interruptions the medullary sheath shows a variable number of oblique clefts (Schmidt) (figs. 184, 186), subdividing it into irregular portions, which have been termed *medullary segments*; but there is reason to believe that the clefts are artificially produced. At the clefts there is an appearance of spiral fibres in the medullary sheath, especially after treatment of the nerve with certain reagents (Golgi); it is, however, probable that this appearance also does not represent a pre-existing structure. A reticular appearance has also been noticed in the medullary sheath (*neurokeratin network* of Kühne, fig. 187),

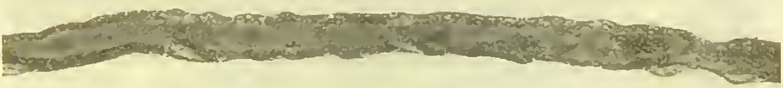

FIG. 186.—NERVE-FIBRE PREPARED WITH OSMIC ACID. Photograph. A constriction of Ranvier is seen on the right. The intervals between the medullary segments appear as clear oblique lines.

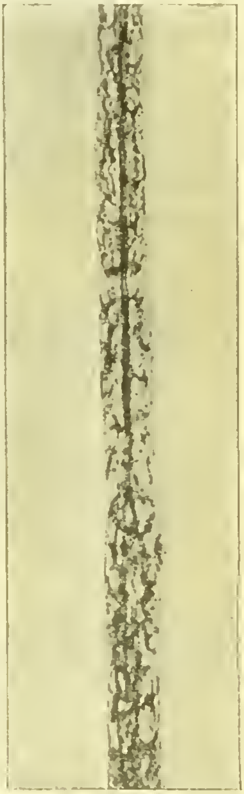

FIG. 187.—RETICULUM OF NEUROKERATIN IN MEDULLARY SHEATH OF NERVE-FIBRE. Photograph. Magnified 600 diameters.

and can be readily seen in nerve-fibres fixed in alcohol and treated with ether, but it varies greatly in aspect, and is perhaps produced by the action of the reagents employed to show it. By other modes of fixation (*e.g.* picric acid) the medullary sheath seems to have a rod-like structure (fig. 189); this again may be due to the manner in which certain of its constituents are coagulated by the reagent, Osmic acid stains the medullary sheath black (figs. 186, 188).

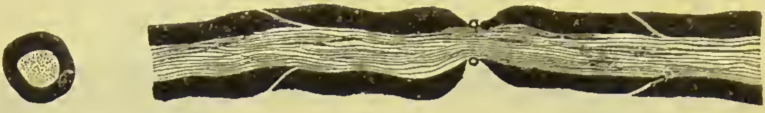

FIG. 188.—LONGITUDINAL AND TRANSVERSE SECTION OF MEDULLATED NERVE-FIBRE OF FROG (OSMIC ACID AND ACID FUCHSINE). (After Biedermann.)

The longitudinal section shows one node of Ranvier and two medullary clefts. The fibrillar structure of the axis-cylinder is shown in both longitudinal and transverse section.

The *axis-cylinder*, which runs along the middle of the nerve-fibre, is a soft transparent thread which is continuous from end to end of the nerve. On account of the peculiar refractive nature of the medullary sheath it is difficult to see the axis-cylinder in the fresh nerve except at the nodes, where it may be observed stretching across the interruptions in the medullary sheath; it may also sometimes be seen projecting from a broken end of a nerve fibre. It is longitudinally striated, being made up of exceedingly fine fibrils (*neuro-fibrils*, fig. 188). They are readily seen at the terminations of nerves as in the cornea and are also visible in the section of a nerve fibre as fine dots (fig. 188), which sometimes appear to have a clear centre (fig. 189), as if the fibrils were tubular. Staining with nitrate of silver produces a curious transversely striated appearance in the axis-cylinder (Frommann) (fig. 196, c), but this is due to the precipitation of chlorides, and does not indicate a pre-existing structure (Macallum).

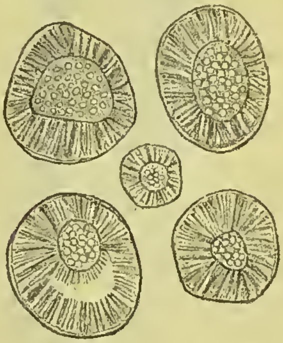

FIG. 189.—SECTION ACROSS FIVE NERVE-FIBRES. Magnified 1000 diameters.

The nerve was hardened in picric acid and stained with picro-carmine. The radial striation of the medullary sheath is very apparent. In one fibre the rays are broken by shrinkage of the axis-cylinder. The fibrils of the axis-cylinder appear tubular. (From a photograph.)

Medullated nerve-fibres vary greatly in size (fig. 190), but may be classified as *large*, *intermediate*, and *small*. The largest are those which are passing to the skin and to the voluntary muscles; the smallest are those which are distributed to the viscera and blood-vessels by way of the autonomic nerves.[1] As shown by Gaskell, the anterior roots of the last one or two cervical nerves, of all the thoracic, of the first and second lumbar, and of the second and third sacral nerves contain besides the ordinary large medullated fibres a bundle of very small medullated fibres which are destined for the viscera and blood-vessels, and which for the most part pass to the sympathetic system. The roots of some of the cranial nerves (the spinal accessory, vagus, glosso-pharyngeal, and facial) contain similar fine medullated fibres.

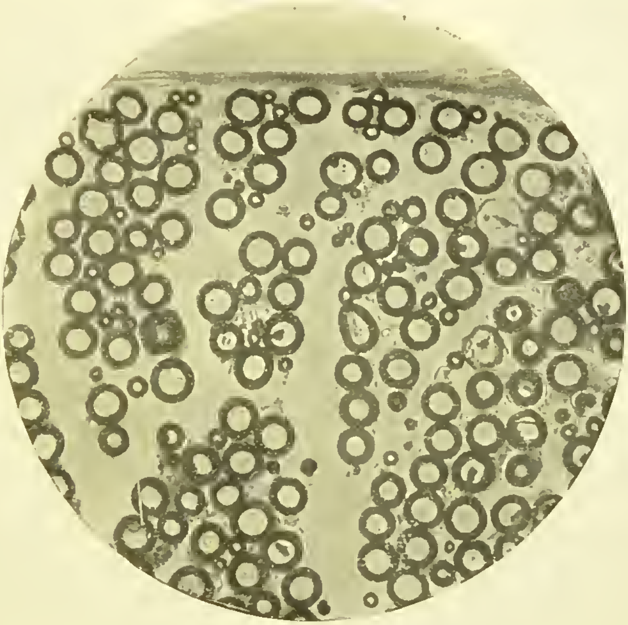

FIG. 190.—SECTION OF THE SCIATIC NERVE OF A CAT, SHOWING THE VARIATIONS IN SIZE OF ITS CONSTITUENT FIBRES. Photograph. Magnified 300 diameters. The nerve was fixed with osmic acid.

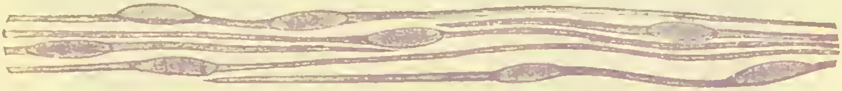

FIG. 191.—NON-MEDULLATED NERVE-FIBRES. Magnified 400 diameters.

Non-medullated fibres.—Intermingled with the medullated fibres there may always, even in the cerebro-spinal nerves, be found a certain number of pale fibres devoid of the distinct double contour which is characteristic of the presence of a medullary sheath. These are the *grey* or *non-medullated fibres*, also called, after their discoverer, *fibres of Remak* (fig. 191). They frequently branch, which the medullated fibres rarely do except near their termination, and they are beset with numerous nuclei which have usually been regarded as belonging to a delicate sheath, although, as a matter of fact, both in longitudinal view and in cross section the nuclei appear to lie in the substance of the fibres. The sympathetic nerves, as they approach their peripheral distribution, are largely made up of fibres of this nature, but the pre-ganglionic fibres of the sympathetic possess a thin medullary sheath, and have the usual structure of medullated fibres.

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[1] This term has been introduced by Langley to include both the nerves of the sympathetic system and also the analogous nerves which proceed from the cranial and sacral regions for the innervation of certain involuntary muscles and secreting glands.

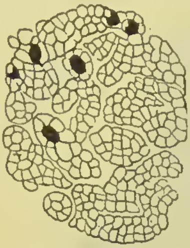

Fig. 192.—Section across non-medullated fibres from the splenic nerve of the ox. (Tuckett.)

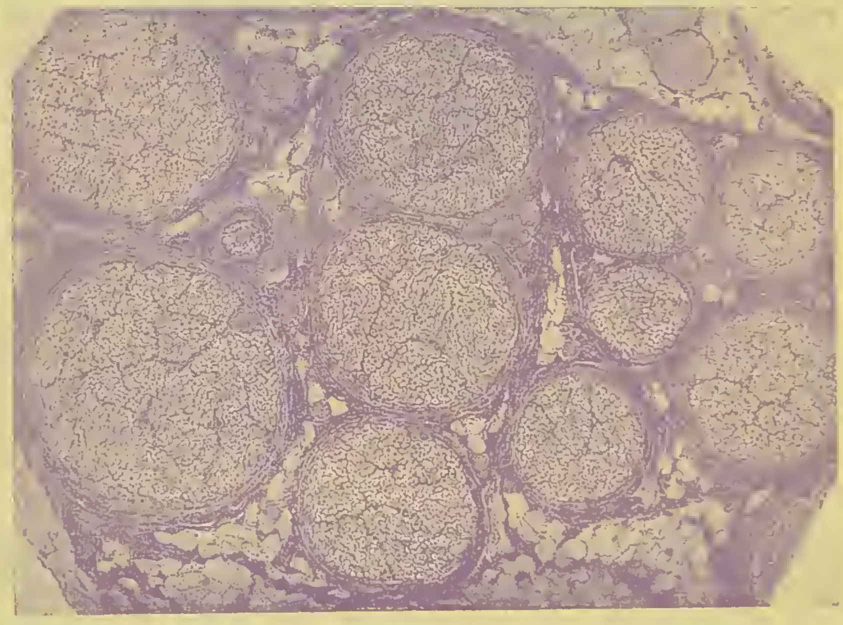

Fig. 193.—Section of part of sciatic nerve of man. (Photograph.) Magnified 60 diameters.

Three funiculi are shown. The fat-cells in the epineurium appear as clear spaces. Blood-vessels are also seen in the epineurium.

Structure of the nerve-trunks.—In their course through the body the nerve-fibres are gathered up into *bundles* or *funiculi*, and the funiculi are again united together to form the nerves which we meet with in dissection. The connective tissue which unites the funiculi and invests the whole nerve, connecting it to neighbouring parts and conveying to it blood-vessels, lymphatics, and even nerve-fibres destined for its coats,

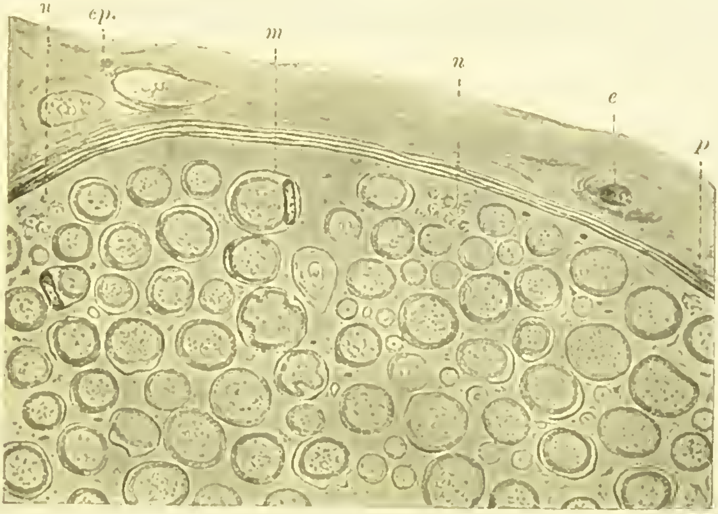

FIG. 194.—SECTION OF PART OF A FUNICULUS OF THE SCIATIC NERVE OF A CAT FIXED WITH FLEMMING'S SOLUTION. Magnified 400 diameters.

ep, epineurium with blood-vessels; *e*, section of an end-bulb; *p*, perineurium; *m*, medullated fibre cut at the level of a nucleus; **n**, **n**, bundles of non-medullated fibres.

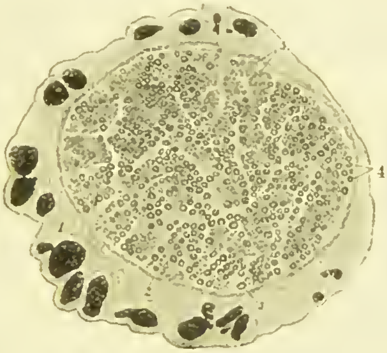

FIG. 195.—SECTION OF THE THORACIC SYMPATHETIC CORD OF THE CAT. (Fischer.) Osmic preparation.

The nerve is composed in almost equal parts of fine medullated fibres (3, 4) derived from the thoracic anterior roots, and grey fibres (5) derived from the sympathetic ganglion-cells. The dark bodies in the epineurium (1) are fat-cells; 2, perineurium.

is termed the *epineurium*; it frequently contains fat-cells. That which ensheathes the funiculi is known as the *perineurium* (figs. 193, 194). It has a distinctly lamellar structure, the lamellæ being composed of connective tissue covered by flattened epithelioid cells (fig. 196, A).

Between the lamellæ are clefts for the conveyance of lymph to the lymphatics of the epineurium. The delicate connective tissue which lies between the nerve-fibres of the funiculus is the *endoneurium*. It assists in supporting the longitudinally arranged meshwork of blood-capillaries, and its interstices communicate with the lymph-clefts of the perineurium.

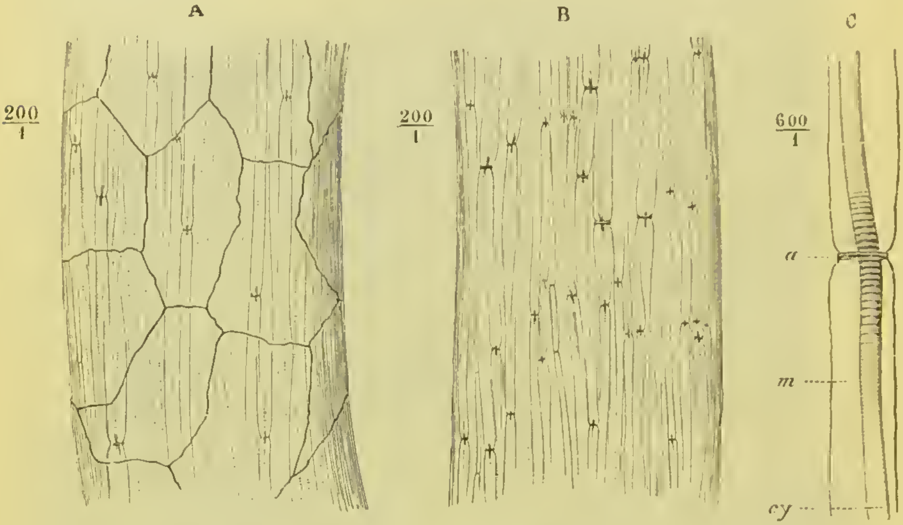

FIG. 196.—NERVES STAINED WITH SILVER NITRATE. (Ranvier.)

In A, the epithelial-like layer of flattened cells belonging to the sheath of Henle is stained. In B, the cross-like markings at the nodes are exhibited. In C, a single fibre is shown more highly magnified, with Frommann's transverse markings of the axis-cylinder. *a*, constricting band; *m*, medullary sheath; *cy*, axis-cylinder.

All the branches of a nerve, and even single nerve-fibres which are passing to their distribution, are invested with a prolongation of the perineural sheath, which is then known as the *sheath of Henle*.

The nerve-trunks themselves receive sensory nerve-fibres (*nervi nervorum*) which ramify chiefly in the epineurium and terminate within this in end-bulbs (Horsley) (fig. 194, *e*).

The degenerative processes which occur in cut nerve-fibres as well as the subsequent reparative processes will be dealt with after the structure of nerve-cells has been studied (see p. 177).

LESSONS XVII. AND XVIII.

NERVE-CELLS.

1. Put a small fragment of spinal ganglion into 1 per cent. osmic acid for a few hours. Place in water containing a fragment of thymol for two days or more. Tease in dilute glycerine. Notice the spheroidal ganglion-cells; their large nuclei and distinct nucleoli. Many of the cells may still be seen within their nucleated membranous sheath. Look for cells which still retain the axis-cylinder process and for T-shaped junctions of nerve-fibres with this. Fat-cells may be present in the periganglionic connective tissue. These will appear intensely black in osmic preparations.

2. Prepare in the same way a spinal ganglion or the Gasserian ganglion of the skate or cod. Notice the bipolar character of most of the cells.

3. Prepare a piece of sympathetic ganglion as in §§ 1 and 2. If from a rabbit observe that many of the cells are bi-nucleated.

Measure two or three cells in each of the above preparations.

4. Mount stained sections of ganglia, both spinal and sympathetic. These will serve to show the arrangement of the cells and fibres in the ganglion and the nucleated sheaths around the nerve-cells.

The ganglia may be fixed and hardened in saturated solution of corrosive sublimate or of picric acid or in 10 per cent. formol. They may either be stained in bulk or sections cut from paraffin and stained on the slide.

5. Ehrlich's methylene blue method, Golgi's silver chromate method, or Cajal's silver reduction method, especially the last named, are all useful for showing the connections of ganglion-cells with nerve-fibres. These methods are described in the Appendix.

6. Place a portion of the grey matter from a piece of spinal cord in 33 per cent. alcohol. After macerating for a few days in this fluid, a little of the grey matter may be shaken up in a test-tube with water so as to break it up into fine fragments. Allow these to subside, decant off the water and substitute a dilute solution (1 to 500) of methylene blue or a solution of picrocarmine. When it appears sufficiently stained some of the debris is pipetted off and examined under a low power of the microscope; at first without a cover-glass so that the cells may, if necessary, be separated with needles from the rest of the tissue. Mount in water with a thick hair under the cover-glass. Notice the large branching cells, some with a mass of pigment near the nucleus. Observe the fibrillation of the cell-processes. Many axis-cylinders will be seen in this preparation deprived wholly or partially of their medullary sheath, and their fibrillar structure can then also be well seen. Carefully sketch these appearances. To keep the methylene-blue preparation the stain must be fixed with picrate of ammonia, after which a mixture of glycerine and picrate of ammonia may be used for mounting. If picrocarmine is used the specimen is simply preserved in dilute glycerine. Similar preparations may be made from the grey matter of the cerebral cortex and cerebellar cortex.

7. Examine sections of spinal cord, medulla oblongata and brain stained by methylene blue (Nissl's method), to exhibit the angular particles within the nerve-cells.

8. Examine sections of parts of brain, spinal cord and ganglia prepared by Cajal's method, to exhibit the neuro-fibrils in the cells and cell processes.

9. Examine the nerve-cells and neuroglia-cells in sections from the spinal cord, cerebrum, or cerebellum of a small animal, *e.g.* young rat or kitten, prepared by Golgi's method. The sections must be mounted in thick xylol balsam or dammar varnish, without a cover-glass, and dried rapidly on a warm plate.

10. Examine sections of spinal cord (lumbar enlargement) and corresponding spinal ganglia from an animal in which the sciatic nerve had been cut about three weeks before it was killed. The sections are to be stained by Nissl's method. Most of the anterior horn nerve-cells and of the ganglion-cells on the side of the lesion will exhibit chromatolysis (or breaking down of the Nissl granules) which is characteristic of cells the axons of which have been severed. The altered cells may be compared with the normal cells on the intact side.

Nerve-cells, neurocytes or neurones.—Nerve-cells occur in the grey matter of the nerve-centres, and in little groups on the course of certain of the peripheral nerves, these groups often causing nodular enlargements of the nerves, which are known as *ganglia.* The most conspicuous ganglia are those which are found upon the posterior roots of the spinal nerves, upon the roots of some of the cranial nerves, and upon the trunk and principal branches of the sympathetic nerve. Minute ganglia are also found very numerously in connection with the nerves which are supplied to glands and involuntary muscular tissue, as in the salivary glands, heart, alimentary canal, bladder, uterus, etc.

Nerve-cells vary much in size and shape; many are large, some being amongst the largest cells met with in the body, but others are quite small. The cell-body, which is often erroneously spoken of as the nerve-cell, but which may be conveniently termed the *cyton* (Sanger Brown), has a large usually spherical nucleus and a very distinct nucleolus. All nerve-cells possess at least one process, the *axon*, which becomes either a non-medullated fibre or the axis-cylinder of a medullated fibre. If other processes are present they are always branched almost from their commencement at the cell-body, and they are therefore termed *dendrons* or *dendrites.* The cytoplasm is fibrillated, the fibrils passing into the processes; they are known as *neuro-fibrils*, and are believed to be the actual conductors of nerve-impulses. The cytoplasm also contains peculiar angular particles (*Nissl granules*) staining deeply with methylene blue, but the size, number, and arrangement of these in different cells vary greatly (fig. 197). The granules also vary in numbei and size with the physiological condition of the cells; thus it is found that nerve-cells which have been fatigued by prolonged activity (fig. 198), and also those the axis-cylinder

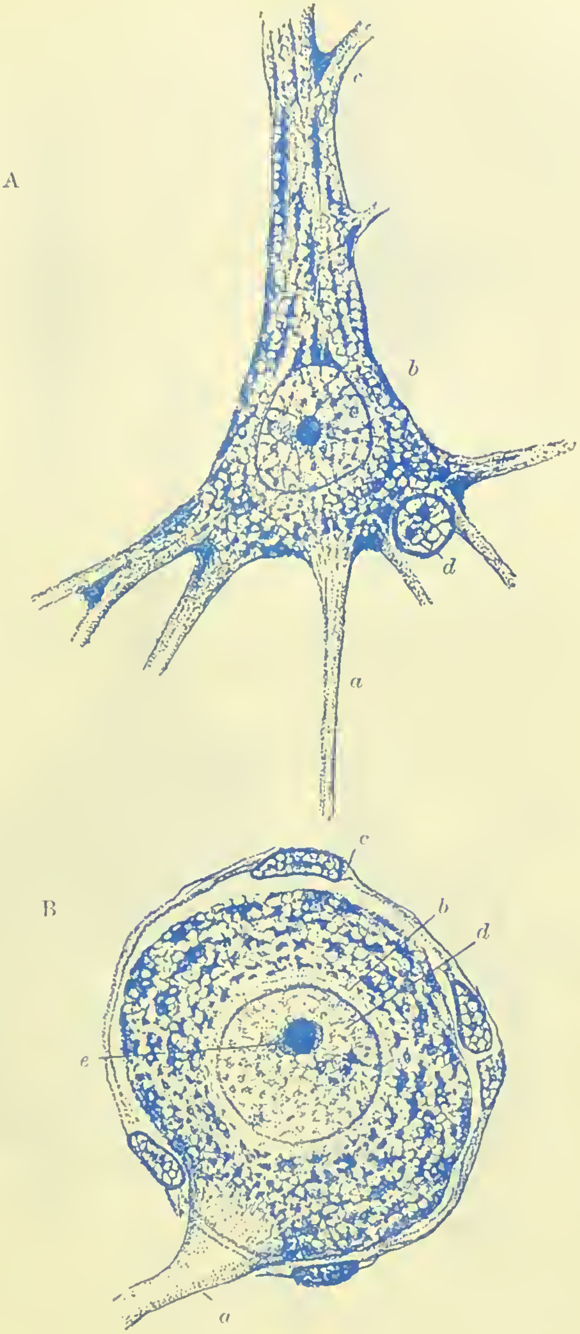

Fig. 197.—Multipolar and unipolar types of nerve-cell.

A, Large pyramidal cell of cerebral cortex, human. Nissl method. (Cajal.) *a*, axon; *b*, cyton; *c*, apical dendron; *d*, placed between two of the basal dendrons points to the nucleus of a neuroglia cell which is applied to the cyton.

B, Unipolar cell from spinal ganglion of rabbit. Nissl method. (Cajal.) *a*, axon; *b*, circumnuclear zone, poor in granules; *c*, capsule; *d*, network within nucleus; *e*, nucleolus.

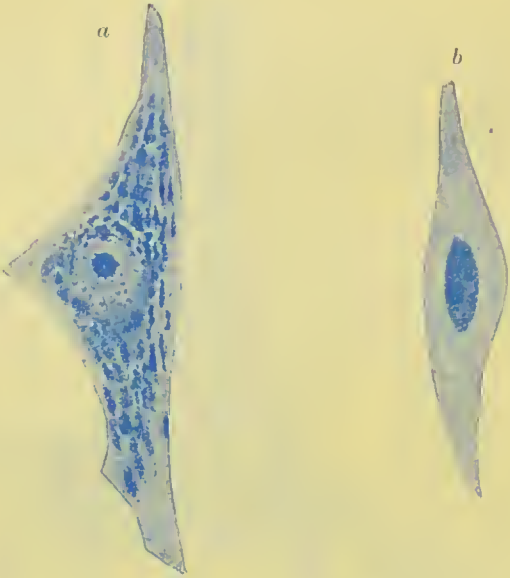

FIG. 198.—TWO MOTOR NERVE-CELLS FROM THE DOG.

a, normal; *b*, after a period of prolonged activity. (Photographed from preparations by Dr Gustav Mann.)

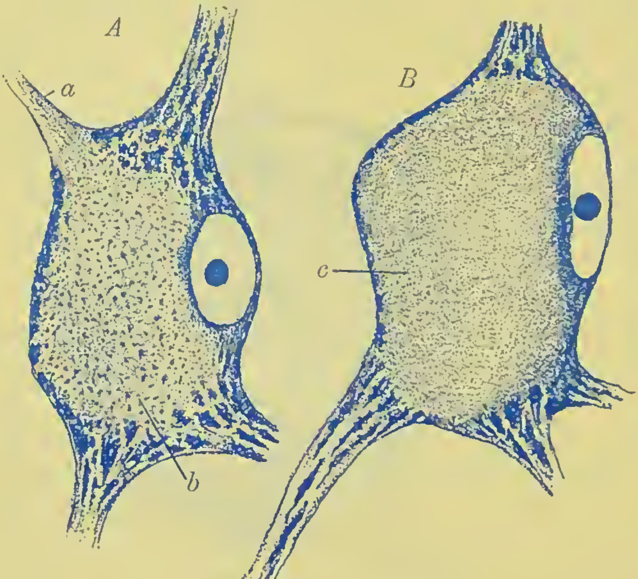

FIG. 199.—CHROMATOLYSIS OF TWO NERVE-CELLS OF SPINAL CORD OF RABBIT, PRODUCED BY SEVERANCE OF MOTOR NERVE 15 DAYS PREVIOUSLY. (Cajal.)

A, the chromatolysis is rather less advanced than in B. In both the nucleus is displaced to the periphery. *a*, axon; *b*, *c*, chromatolysed cell-substance. A completed condition of chromatolysis is seen in fig. 198 *b*.

process of which has been cut (fig. 199), show the Nissl granules becoming disintegrated; they may even disappear for a time from the cell. A similar result is found to occur after the action of poisons which especially affect the nervous system. The Nissl granules of the nerve-cell appear to consist chemically mainly of nucleoproteid; they contain organically combined iron (Macallum). Many nerve-cells have also a clump of pigment-granules (fig. 200), containing lecithin, at one side of the nucleus. This is especially marked in certain localities (locus cœruleus, locus niger), and is more frequent in man than in the lower animals. The pigment also tends to increase in amount as age advances. As already stated, the body of every nerve-cell is traversed by fine fibrils (*neuro-fibrils*) continuous with those in the axis-cylinder of the issuing nerve and with similar fibrils in their dendrons. They were noticed by Max Schultze in vertebrates and were later described by Aápthy in certain annelids. They can be seen without difficulty in nearly all nerve-cells (fig. 201)

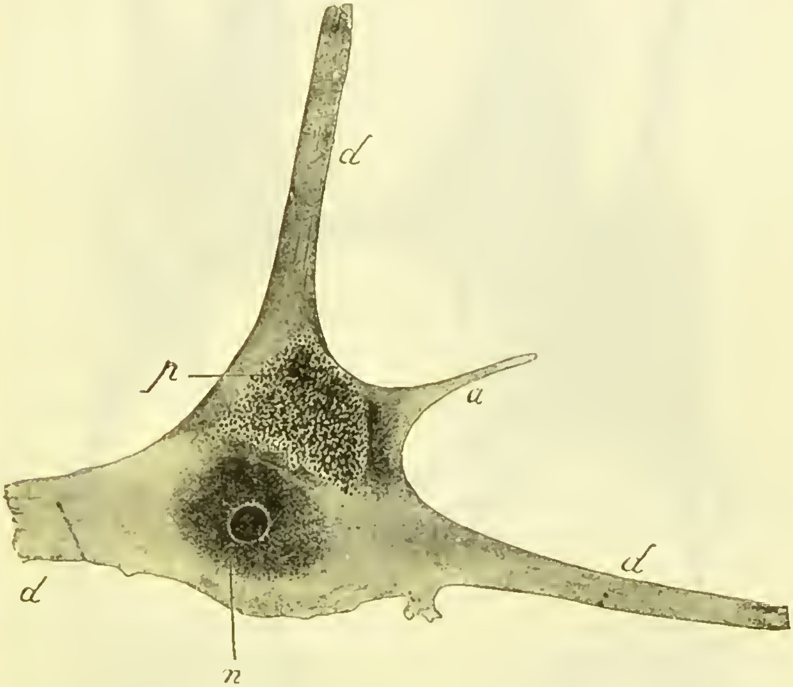

FIG. 200.—A NERVE-CELL FROM THE HUMAN SPINAL CORD. (From Prenant, Bouin, and Maillard.)

a, axon; *d*, dendrons; *n*, nucleus with nucleolus; *p*, pigment-granules.

by the employment of certain special methods. The neuro-fibrils are said to present variations in thickness according to the condition of activity of the animal at the time of death.

Most, if not all, nerve-cells show a delicate *superficial reticulum* (fig. 202), described by Golgi, which is generally regarded as composed of neuro-fibrils, but, according to J. Turner, may be an investment derived from neuroglia-cells. Golgi has also described another network of fibrils with somewhat larger meshes (*deep reticulum* of Golgi) (fig. 203) in the deeper parts of the cell. According to some authorities both superficial and deep networks are in continuity

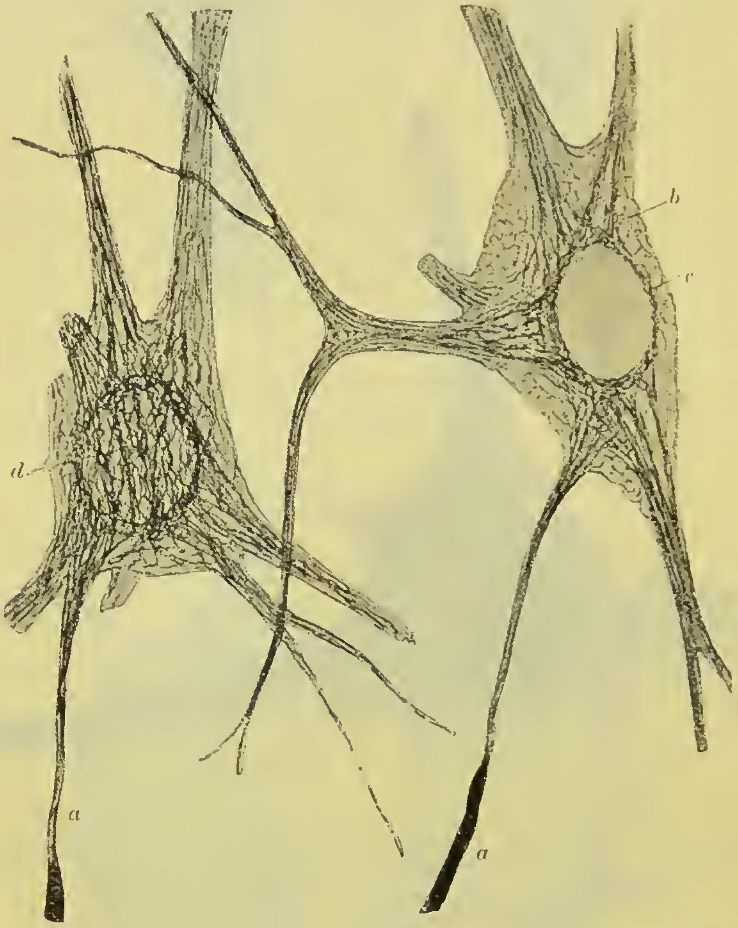

FIG. 201.—NERVE-CELLS OF KITTEN (FROM THE ANTERIOR CORPORA QUADRIGEMINA) SHOWING NEURO-FIBRILS. (Cajal.)

a, axon ; *b*, *c*, *d*, various parts of the intracellular plexus of fibrils.

throughout the cell, and receive and are prolonged from the neurofibrils of an entering axon on the one hand, and with those of the

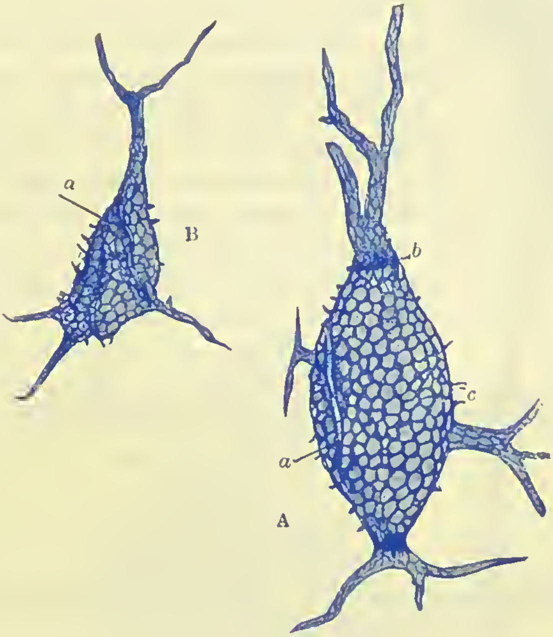

FIG. 202.—SUPERFICIAL NETWORK OF GOLGI SURROUNDING TWO CELLS FROM THE CEREBRAL CORTEX OF THE CAT; EHRLICH'S METHOD. (Cajal.)

A, large cell; B, small cell. *a*, *a*, folds in the network; *b*, a ring-like condensation of the network at the poles of the larger cell; *c*, spinous projections from the surface.

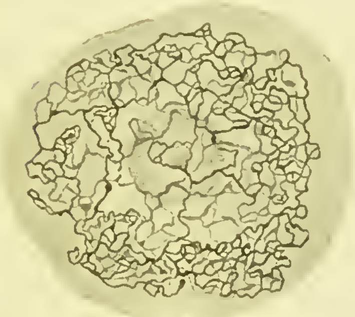

FIG. 203.—NERVE-CELL FROM SPINAL GANGLION, SHOWING NETWORK AROUND THE NUCLEUS. (Golgi.)

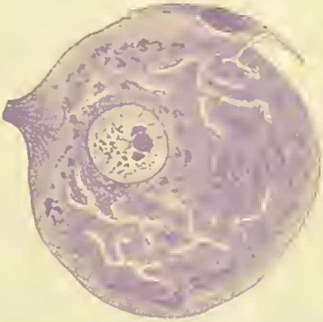

FIG. 204.—TROPHOSPONGIUM WITHIN A GANGLION-CELL. (E. Holmgren.)

axis-cylinder process of the nerve-cell, and also of the dendrons, on the other hand. Other authorities regard these networks as distinct from the neuro-fibrils, which they suppose to run independently through the nerve-cell body, entering it by way of the dendrons and emerging in the axon.

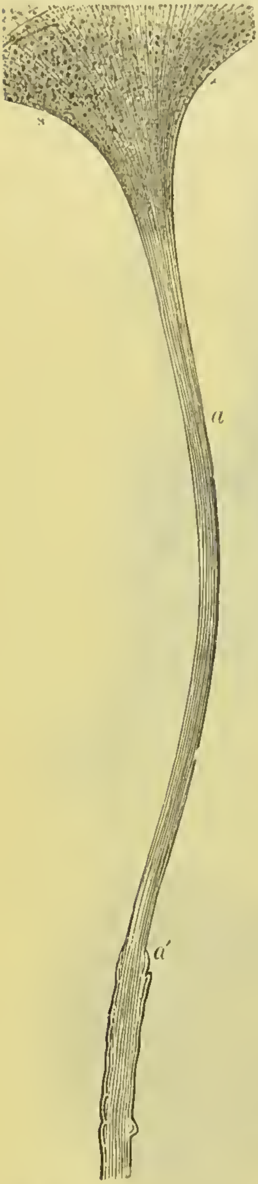

Fig. 205.—Axis-cylinder process of a nerve-cell from the spinal cord. (M. Schultze.) × ×, portion of the cell-body, out of which the fibrils of the axis-cylinder process, *a*, are seen to emerge. At *a′*, this process acquires a medullary sheath. Highly magnified.

Entirely distinct from the fibrils is a system of fine canaliculi, which has been described by E. Holmgren, permeating the cytoplasm of the cell-body in some nerve-cells for the purpose of subserving its nutrition by conveying plasma into its substance (fig. 204). These channels are stated by Holmgren to be occupied by branching processes of neurolgia-cells (*trophospongium*). In the very large nerve-cells from which the nerves of the electric organs of Malapterurus arise, even blood-vessels penetrate into the cytoplasm.

Processes of nerve-cells.—As already intimated the processes are of two kinds. The first is that known as the *axis-cylinder process* (Deiters) or *nerve-fibre process*, so called because it becomes the axis-cylinder of a nerve-fibre (fig. 205, *a*, *a′*); in the case of the non-medullated fibres, it becomes the nerve-fibre itself. It is also termed the *axon.*

No fully developed nerve-cell is without this process. The place where it arises from the body of the nerve-cell (*cone of origin*) is marked off from the rest of the cell-substance by absence of Nissl granules (see fig. 197). The other processes of the nerve-cell are those which were termed by Deiters the *protoplasmic processes*; they are now usually termed the *dendrons* or *dendrites* and are generally multiple, whereas the axon is generally single. The dendrons are characterised by the fact that as soon as they leave the cell they begin to branch dendritically, whereas the axis-cylinder process does not branch until near its termination, with the exception of a few fine lateral offshoots, which are sometimes given off in its course. Dendrons may be absent; the cell is then adendric. Most nerve-cells have only one nerve-fibre process (*unipolar*), but some have two or more (*bipolar*, *multipolar*). The dendrons may contain Nissel granules, but the axons never.

The shape of the cell depends largely on the number of processes and the manner in which they come off from the cell. If there is but one chief process the cell is generally nearly spherical. This is the case with most of the cells of the spinal ganglia (fig. 197, B); in these the single process, after a short course, divides into two fibres, which pass the one centrally the other peripherally (fig. 216). When there are two main processes from a nerve-cell they often go off in opposite directions from the cell, which is thus rendered somewhat spindle-shaped (fig. 206), but occasionally they emerge at the same part. When there are three or more processes, the cell becomes irregularly angular, as in the motor-cells of the spinal cord and the pyramidal cells of the cerebral cortex (figs. 200, 197, A).

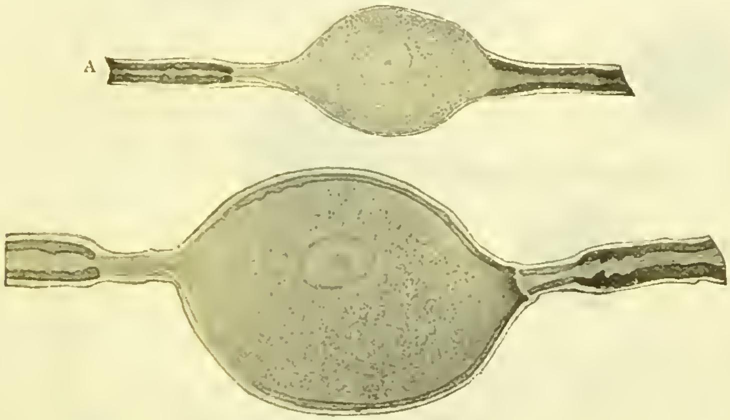

FIG. 206. TWO BIPOLAR GANGLION-CELLS (FISH). (Holmgren.)
In B the medullary sheath is continued as a thin layer over the cell-body.

In some cases where there appear to be two fibres connected with a cell, one of them is derived from another nerve-cell elsewhere, and is passing to end in a ramification which envelopes the cell-body. In certain situations the ramification is coarse and forms a calyx-like investment to the cell-body: this investment may be so intimately united to the body of the second cell that it appears to be rooted into the external layer (fig. 207): in other places the pericellular fibrils are very fine and form a fine arborisation over the cell-body. When the fibrils come in contact with the surface of the cell they sometimes end in small button-like enlargements or varicosities (fig. 208).

In preparations made by Golgi's chromate of silver method the nerve-cells and their processes are coloured black by a deposit of reduced silver, so that the processes can be traced for a considerable distance from the body of the cell, in fact in many instances as far as their remotest ramifications. It has been found by the employment of this method that the axis-cylinder process is not always an un-

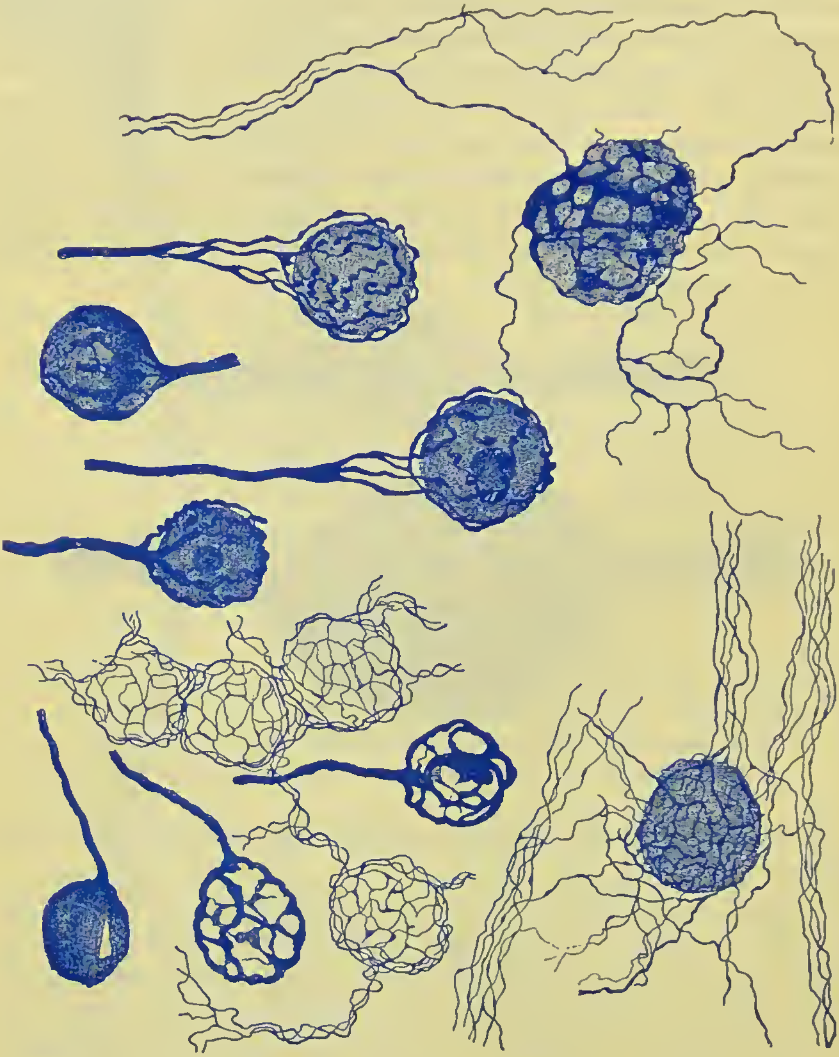

FIG. 207.—VARIOUS FORMS OF PERICELLULAR ENDING OF ENTERING NERVE-FIBRES IN THE TRAPEZOID NUCLEUS OF THE CAT. (Edinger, after Veratti.)

branched process, as was formerly supposed, but that it usually, if not invariably, gives off fine lateral branches (*collaterals*), which themselves tend to ramify in the adjacent nerve-substance (fig. 209, *c*). And although the main part of the axon process usually passes on and becomes the axis-cylinder of a long medullated nerve-fibre (long axoned-cell, fig. 209), this is not always the case, for in another type of nerve-cell within the nerve-centres (short axoned-cell, fig. 210), the axis-cylinder process breaks up almost immediately into an arborescence. The long process of the first type (which becomes the axis-cylinder of a long nerve-fibre) also ultimately ends in a similar manner, that is to say, in a terminal ramification or arborescence, as will be seen in studying the endings of nerve-fibres, both at the periphery and within the central nervous system itself.

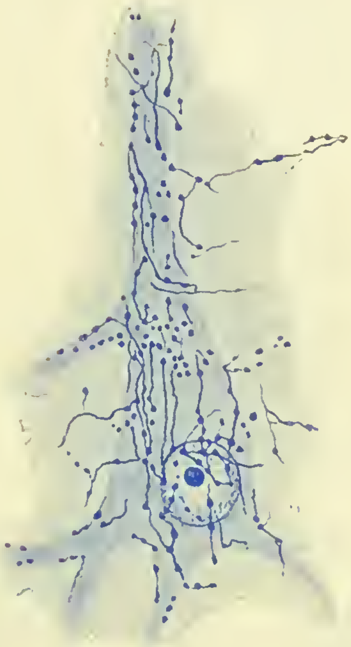

FIG. 208.—PERICELLULAR NEURO-FIBRILS AROUND A LARGE PYRAMIDAL CELL OF THE HUMAN CORTEX CEREBRI.[1]

Synapses.—Each nerve-cell is generally regarded as an anatomically independent element (*nerve-unit*, *neurone*), and the connection of one nerve-cell with another is believed to be effected through the medium of the terminal arborisations of the dendrons or axons. Such arborisations from different cells may interlace with one another (as in the olfactory glomeruli, in the retina, and in the sympathetic ganglia) (fig. 211), or a terminal arborisation from one cell may embrace the body or the cell-processes of another cell; as with the cells of the spinal cord (fig. 212) and the cells of the trapezoid nucleus of the pons Varolii

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[1] I am indebted to Dr J. Turner for the drawing here reproduced.

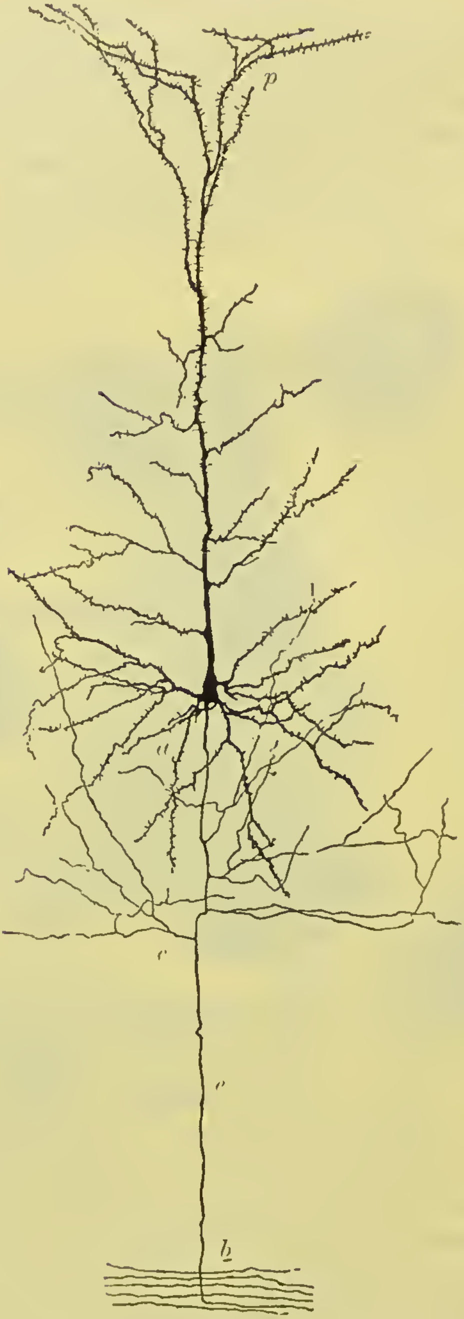

FIG. 209.—A PYRAMIDAL CELL OF THE CORTEX CEREBRI OF THE RABBIT. (Cajal.)

a, basal dendrons; *p*, apical dendron ramifying near surface; *e*, axon; *c*, its collaterals; *b*, fibres of white matter of brain.

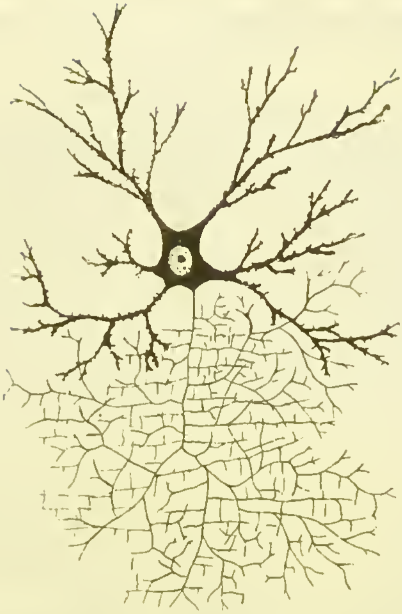

FIG. 210.—CELL OF TYPE II. OF GOLGI, WITH SHORT AXON RAMIFYING IN THE ADJACENT GREY MATTER.

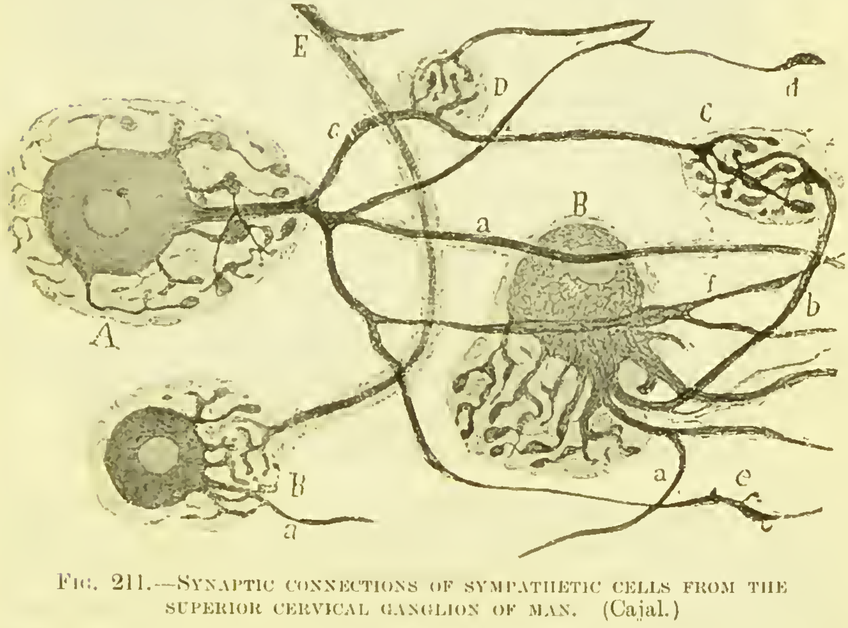

FIG. 211.—SYNAPTIC CONNECTIONS OF SYMPATHETIC CELLS FROM THE SUPERIOR CERVICAL GANGLION OF MAN. (Cajal.)

The cells (A, B) show well-marked intracapsular dendrons. C, D, synapses between dendrons outside the cell-capsules; E, a fibre, which is itself surrounded by a fine spirally wound fibril, passing to a cell and forming a synapse with the cell-dendrons within the capsule. *a*, *a*, axons; *b*, *c*, *d*, *e*, *f*, extra-capsular dendrons.

(fig. 207) and in many other places. The term *synapse* or *neuro-synapse* is applied to these modes of junction. By them nerve-cells are linked together into long *chains of neurones*, the physiological path being uninterrupted, although the anatomical path is, as above indicated, believed to be interrupted at the synapses.

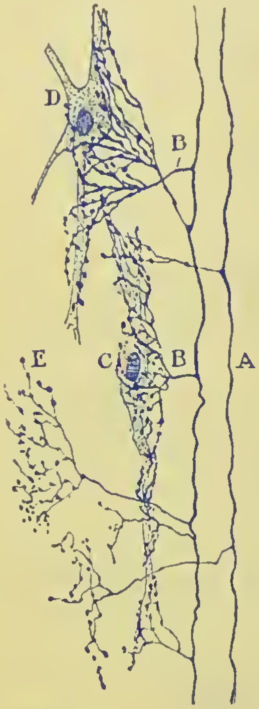

Fig. 212.—Arborisation of collaterals from the posterior root-fibres around cells in the posterior horn of grey matter. (Cajal.)

A, fibres of posterior column derived from posterior root; B, collaterals; C, D, nerve-cells in grey matter surrounded by the arborisations of the collaterals; E, an arborisation shown separately.

The doctrine of the anatomical independence of the nerve-cell is known as the "neurone-theory" (Waldeyer). It is supported by the appearances of chromate of silver preparations of nerve-cells. In these the reduction of the silver is strictly confined to single cells, which become stained with all their processes; and these processes, when demonstrated by this method, are never found in continuity either with the processes or with the bodies of other nerve-cells. Moreover, many of the facts relating to nerve-degeneration can be more readily interpreted by this theory than by one which assumes the existence of direct continuity between the nerve-units. But it has been shown by Apáthy that in annelids (the nervous system of which was formerly supposed to offer a typical example of isolated, linked "neurones"), the fibrils are in fact continuous from cell to cell and are not interrupted at the synapses; it is therefore possible that the same may prove true for vertebrates also, in which case the doctrine of independent units would require modification. We may at any rate assume the truth of the hypothesis so far as the *nutrition* of all the processes of the nerve-cell to their remotest termination is concerned, independently of the question whether there is or is not anatomical continuity of nerve-fibrils from one unit to the other; for there are many examples in both animal and plant cells of such interdependence by means of fibrils, combined with a considerable amount of trophic independence.

STRUCTURE OF GANGLIA.

In the **ganglia** (figs. 213, 214) each nerve-cell has a nucleated sheath which is continuous with the neurolemma of the nerve-fibre with which the cell is connected. In the **spinal ganglia**, and in many of the corresponding ganglia on the roots of the cranial nerves of mammals and of most other vertebrates, the cells have only one issuing process, the axis-cylinder process, which soon acquires a medullary sheath and then passes with a somewhat convoluted course to some little distance from the cell-body, where, still within the ganglion, it divides into two; one fibre passing to the nerve-centre, and the other towards the periphery. The branching is T-shaped or Y-shaped, and always occurs at a node

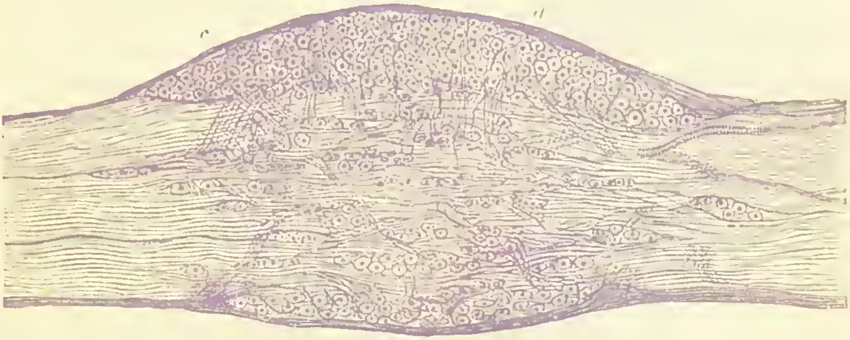

FIG. 213.—LONGITUDINAL SECTION THROUGH THE MIDDLE OF A GANGLION ON THE POSTERIOR ROOT OF ONE OF THE SACRAL NERVES OF THE DOG, AS SEEN UNDER A LOW MAGNIFYING POWER.

a, nerve-root entering the ganglion; *b*, fibres leaving the ganglion to join the mixed spinal nerve; *c*, connective-tissue coat of the ganglion; *d*, principal group of nerve-cells, with fibres passing down from amongst the cells, to unite with the longitudinally coursing nerve-fibres by T-shaped junctions.

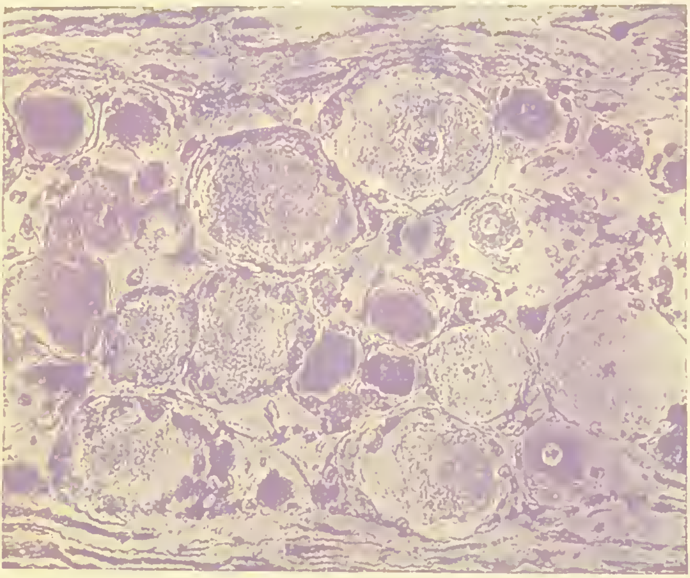

FIG. 214.—FROM A SECTION OF DOG'S SPINAL GANGLION, SHOWING DIFFERENT TYPES OF CELLS. Photograph. Magnified 240 diameters.

The clear patch, free of Nissl granules, seen in some of the cells is the place of origin of the axon. Some of the cell-bodies have shrunk away from the nucleated capsule. Notice the smaller and more darkly staining cells, contrasting with the larger and clearer cells.

of Ranvier (figs. 215, 216). The neuro-fibrils of the central and peripheral branches retain their individuality in the common trunk; they are traceable into a neuro-fibril network within the cell-body. These spinal ganglion-cells have, as a rule, no dendrons, but some show, besides the axon, short processes terminating in bulbous enlargements (fig. 218) either within the cell-capsule or immediately outside it (Huber, Cajal). These either represent dendrons, or, as Nageotti has suggested, aborted axons. The short intracapsular process also occur in sympathetic ganglia (Cajal) (figs. 211, 222).

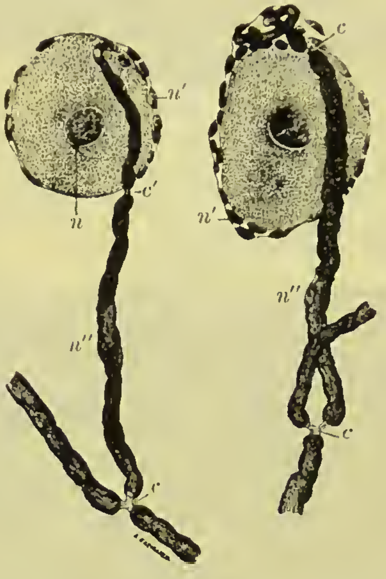

FIG. 215.—TWO SPINAL GANGLION-CELLS, SHOWING BIFURCATION OF THEIR NERVE-FIBRE PROCESSES. (Ranvier.) Osmic preparation.

n, nucleus of one of the cells; *n′*, nuclei of capsules; *n″*, nuclei of neurolemma; *c*, *c*, *c′*, *c′*, constrictions of Ranvier.

The origin of the axon is not always simple, but may be multiple, the several parts forming at first a plexus close to the cell, eventually joining to produce a single axon. This multiple condition tends to become accentuated with age (fig. 219).

Two chief varieties of cell occur in the spinal ganglia, one large and clear, the other small and staining almost uniformly dark (figs. 214, 216). Many more types of cell are, however, distinguishable. As was first shown by Dogiel, the cell-body of the spinal ganglion-cell may be invested by the convoluted ramifications of a fine afferent nerve-fibre (fig. 217), derived either from one of the other cells of the same ganglion or from a cell in a neighbouring sympathetic ganglion. Similar afferent fibres forming pericellular plexuses also occur in the sympathetic ganglia (fig. 223).

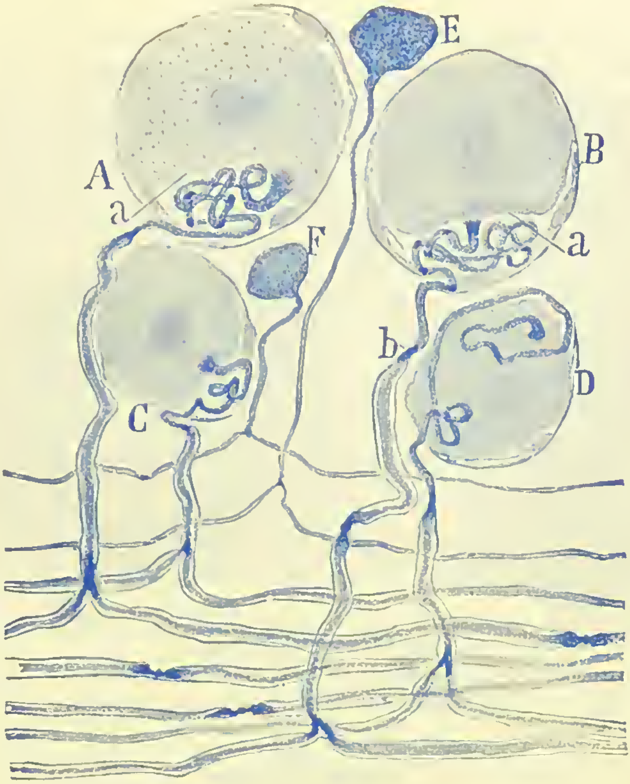

FIG. 216.—TYPES OF CEREBRO-SPINAL GANGLION-CELLS, FROM VAGUS GANGLION OF CAT. (Cajal.)

A, B, large cells with much convoluted commencement of axon ; C, D, smaller cells : E, F, smallest cells, staining darkly and without axonal convolutions.

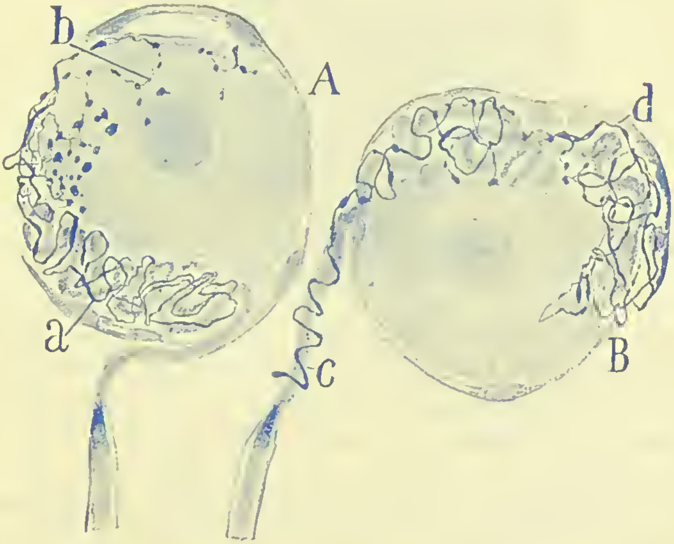

FIG. 217.—PERICELLULAR ARBORISATIONS IN SPINAL GANGLION-CELLS. (Cajal.)

In A the arborisation extends over the cell-body ; in B it is limited to the axon. *a*, *b*, *c*, *d*, afferent fibre.

Sections of **sympathetic ganglia** (fig. 220) fail to show the regular arrangement of bundles of medullated fibres traversing the ganglion which form a conspicuous feature in the spinal ganglia. The nerve-cells are smaller and usually have several dendrons and one axon; this becomes a non-medullated nerve-fibre, but is occasionally finely medullated. In certain animals (rabbit, hare, guinea-pig) the sympathetic cells have each two nuclei (fig. 221). In the frog they are unipolar, but sometimes with a second spiral fibre winding round the issuing axon. Such spiral fibres occur also in man; they appear to be afferent fibres which are forming synapses around the axons and cell-bodies of the ganglia-cells (fig. 223).

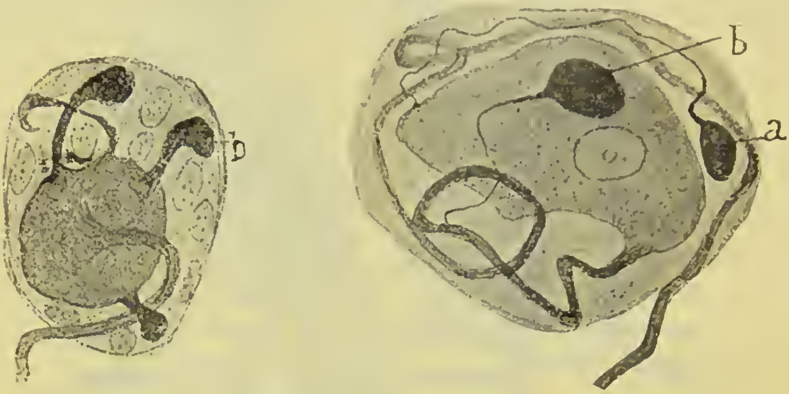

FIG. 218.—CEREBRO-SPINAL GANGLION-CELLS, MAN. (Cajal.)
a, *b*, intracapsular dendrons, with knobbed extremities.

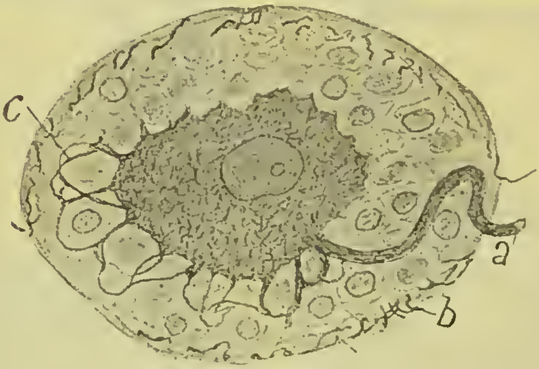

FIG. 219.—SENILE TYPE OF CEREBRO-SPINAL GANGLION-CELL. (Cajal.)
a, issuing axon; *b*, part of pericellular plexus; *c*, pericellular loops.

The cells of ganglia are disposed in aggregations of different size, separated by the bundles of nerve-fibres which are traversing the

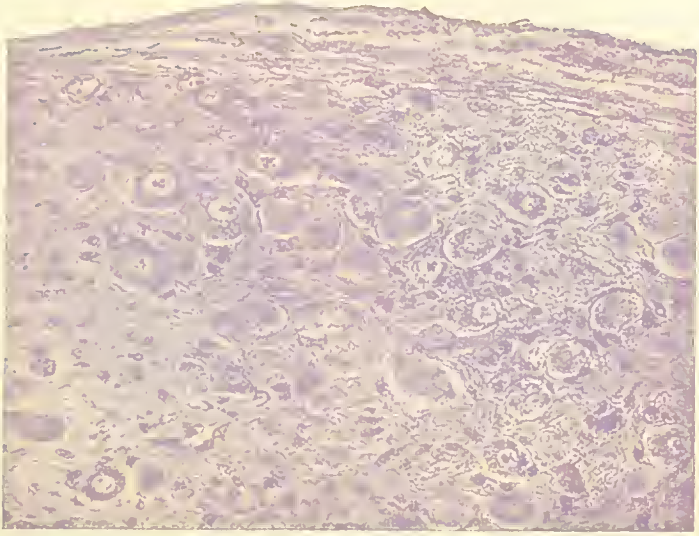

FIG. 220.—SECTION OF SYMPATHETIC GANGLION OF DOG. Photograph. Magnified 240 diameters.

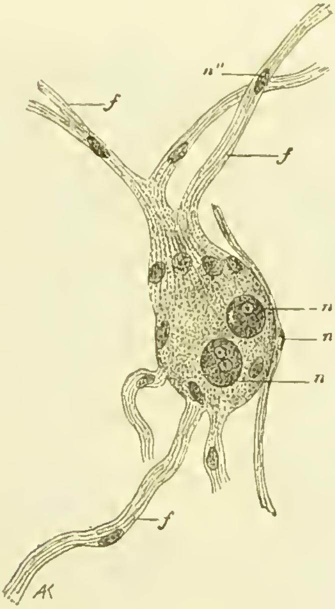

FIG. 221.—A SYMPATHETIC NERVE-CELL. (Ranvier.)
n, *n*, nuclei of cell; *f*, *f*, pale fibres issuing from cell; *n'*, *n''*, nuclei on fibres.

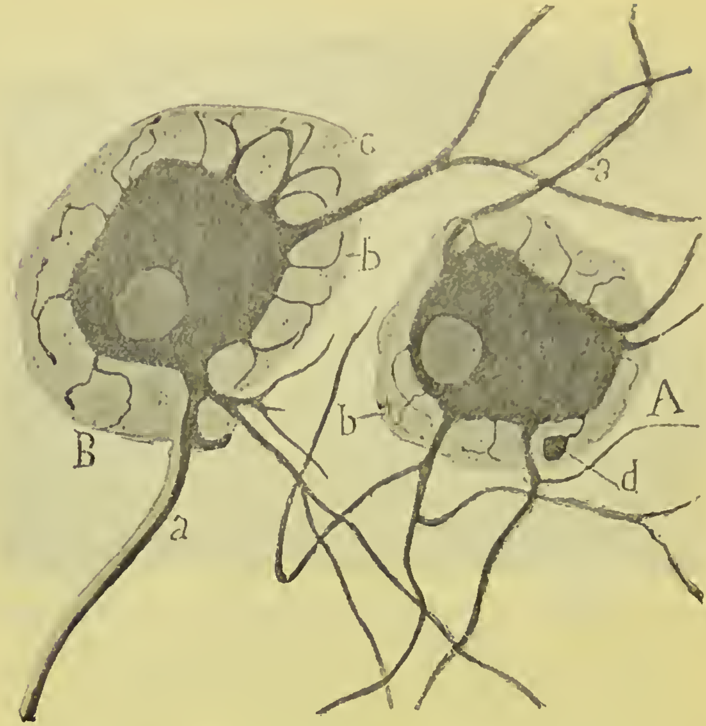

FIG. 222.—TWO SYMPATHETIC CELLS, MAN. (Cajal.)
a, *a*, axon; *b*, *c*, intracapsular processes; *d*, knob-like ending of an intracapsular process.

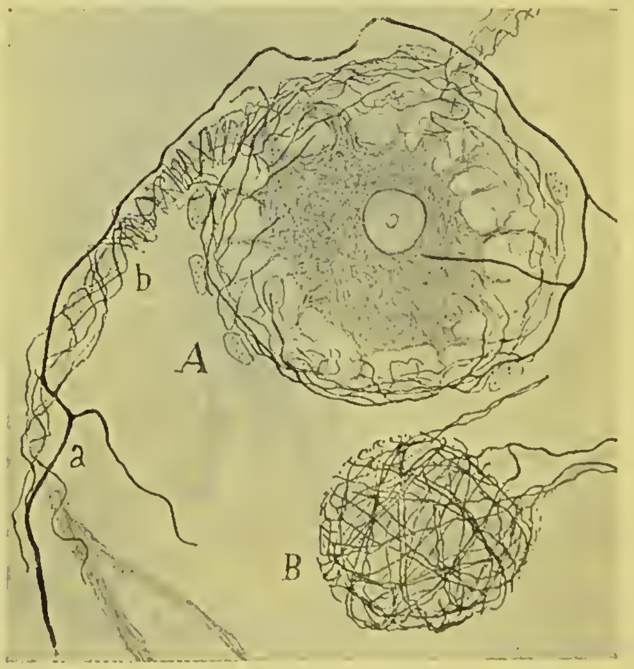

FIG. 223.—TWO CELLS FROM A SYMPATHETIC GANGLION OF MAN SHOWING THE TERMINATION OF AFFERENT FIBRES WITHIN THE CELL-CAPSULE. (Cajal)
A, large; B, small cell. *a*, *b*, afferent fibres surrounding a dendron and passing into capsule.

ganglion (fig. 220). The ganglion if large is enclosed by an investing capsule of connective tissue which is continuous with the epineurium and perineurium of the entering and issuing nerve-trunks.

DEGENERATION AND REGENERATION OF NERVE-FIBRES AND NERVE-CELLS.

Since each nerve-fibre is the process of a nerve-cell, when a nerve is cut, the separated part degenerates. Its axis-cylinder becomes broken up and disappears, the nuclei of the neurolemma multiply, and the medullary sheath undergoes a process of disintegration into droplets of fatty substance which stain intensely, like fat itself, in a mixture of bichromate of potash and osmic acid which does not stain the medullary sheath of normal fibres. The change which results in the fibres was described by A. Waller in 1850, and is known as *Wallerian degeneration* (fig. 224, A to C). In man and mammals these changes begin 24 to 48 hours after section of the nerve, and proceed rapidly, so that by the third day the nerve fibres cease to conduct impulses. When a peripheral nerve is cut, all the nerve-fibres distal to the point of section must degenerate, because all have grown from and are processes of nerve cells in or near the nerve-centre—the afferent fibres from the cells of the ganglion on the posterior root, the efferent fibres from the cells of the anterior horn of the spinal cord.

Waller supposed that no changes are produced centrally to the injury when a nerve is cut, nor indeed is there any obvious immediate alteration in the nerve-fibre itself between the injury and the cell-body, although it is stated that the fibrils of the axis-cylinder disappear for a time. But it was found by Nissl that degenerative changes occur in the cell-body of every cell, whether motor or sensory, the axis-cylinder of which has been severed.[1] These changes become apparent a few days after section of the nerve-fibre and consist in a disintegration of the chromatin granules, associated at first with a general swelling of the cell-body and nucleus, which last passes to the periphery of the cell-body. After a time the disintegrated chromatic substance becomes in great measure removed and the cell-body and nucleus become shrunken in volume. This process of disintegration and disappearance of chromatin may be termed *Nissl degeneration*: it is also known as *chromatolysis*. It is brought about not only by section of the axon (fig. 199), but also as the result of excessive fatigue of the intact cell (fig. 198), and of the action of a large number of drugs and poisons.

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[1] But section of the posterior root-fibres central to the ganglia does not entail degeneration of the ganglion-cells from which they arise. Nor does section of a spinal nerve always entail degeneration of the anterior horn cells from which its motor fibres arise (Van Gehuchten). Why these apparent exceptions occur is not understood.

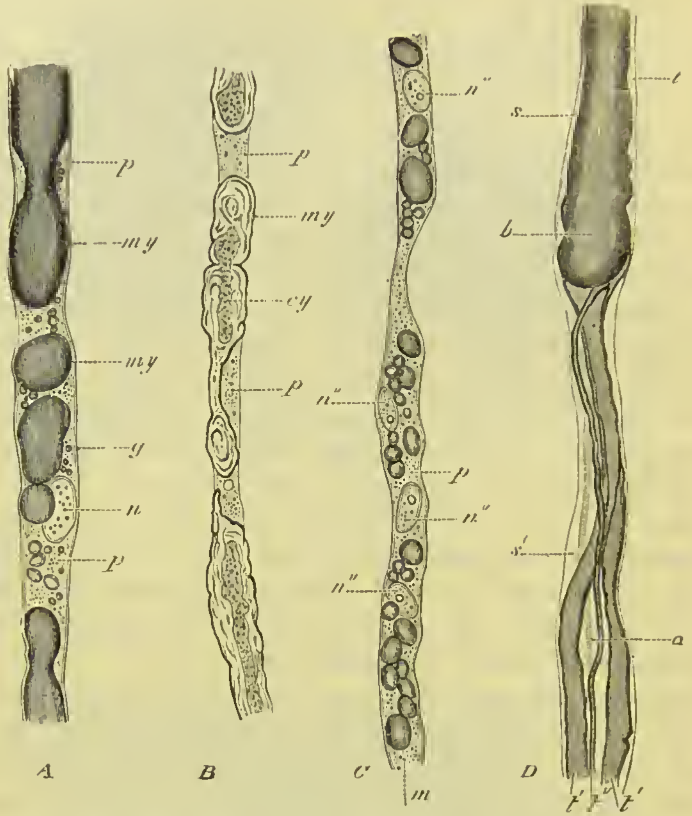

FIG. 224.—DEGENERATION AND REGENERATION OF NERVE-FIBRES IN THE RABBIT. (Ranvier.)

A, part of a nerve-fibre in which degeneration has commenced in consequence of the section, fifty hours previously, of the trunk of the nerve higher up; *my*, medullary sheath becoming broken up into drops of myelin; *p*, granular protoplasmic substance which is replacing the myelin; *n*, nucleus; *g*, neurolemma. *B*, another fibre in which degeneration is proceeding, the nerve having been cut four days previously; *p*, as before; *cy*, axis-cylinder partly broken up, and the pieces inclosed in portions of myelin, *my*. *C*, more advanced stage of degeneration, the medullary sheath having almost disappeared, and being replaced by protoplasm, *p*, in which, besides drops of fatty substance, *m*, are numerous nuclei, *n''*, which have resulted from the division of the single nucleus of the internode. *D*, commencing regeneration of a nerve-fibre. Several small fibres, *t'*, *t''*, have sprouted from the somewhat bulbous cut end, *b*, of the original fibre, *t*; *a*, an axis-cylinder which has not yet acquired its medullary sheath; *s*, *s'*, neurolemma of the original fibre. *A*, *C*, and *D* are from osmic preparations; *B*, from an alcohol and carmine preparation.

The chromatolysis may be persistent or may be recovered from. Sometimes it is followed by almost complete atrophy of the cell-body, and when this is marked there may be a secondary Wallerian degeneration of the part of the nerve-fibre still attached to the cell.

The chromatolysis is accompanied by changes in the neurofibrils of the cells, which stain differently and become granular (Marinesco).

Regeneration.—After a certain lapse of time, especially if the cut ends of the nerve are in apposition, continuity between them may become re-established. But when such regeneration takes place in the cut nerve, it is effected not by a re-establishment of connection between the degenerated fibres and the fibres of the central stump, but by an outgrowth of new fibres from the stump (figs. 224, D; 225), which endeavour to find their way to the periphery along the course of the degenerated fibres. If they succeed in doing so, the continuity and conducting power of the nerve become ultimately restored. This may not happen for three months or more, according to the length of nerve cut off and the nature of the severance, although the process begins within a few days of the injury in man. Some investigators have attempted to show that regeneration may take place independently in the peripheral part of the cut nerve, but the evidence offered is not conclusive, although changes occur in the distal part preparatory to the down-growth of new fibres into it. There appears, in fact, to be no union of the down-growing fibres with regenerated fibres in the peripheral part. Recent investigations have shown conclusively that whenever continuity is re-established it is invariably due to the growth of fibres from the central stump of the cut nerve. These down-growing fibres are usually terminated by a button-like swelling similar to that which characterises the growing fibres of the embryonic nerves (*incremental cone*), and they may also exhibit numerous lateral ramifications. Even when the cut central stump is turned backwards and fixed amongst the muscles or under the skin a certain number of newly-budded fibres may find their way from it into the degenerated peripheral part of the nerve.

If regeneration fail to establish itself, the central end of the cut fibre and the cell-body from which it takes origin undergo slow atrophic changes resulting from disuse. These atrophic changes may ultimately extend to other links in the cell-chain, especially in young animals; so that even remote cells in the same physiological path may eventually become atrophied (*v. Gudden's atrophy*).

No regeneration of cut nerve-fibres is ever seen in the brain or spinal cord, although the process of degeneration of fibres which are cut off from their cell-bodies occurs in the same manner as at the periphery, and the Nissl degeneration also takes place in the cell-bodies. Both in the nerve-centres and the peripheral nerves (if regeneration fail to occur), the place of the degenerated nerve-fibres becomes eventually occupied by strands of fine fibres, somewhat similar to the fibres of cicatricial tissue. These strands stain deeply with carmine and remain unstained by osmic acid and by the Weigert-Pal

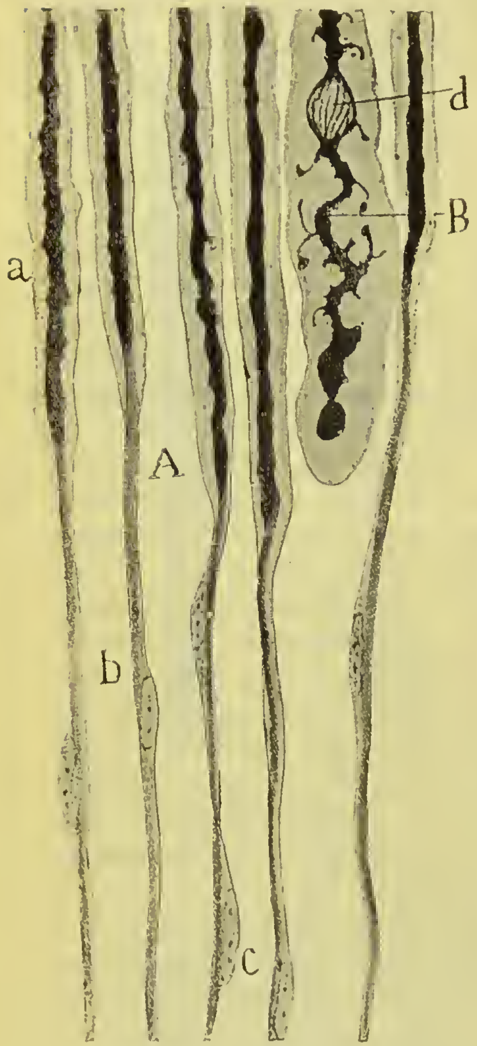

Fig. 225.—Fibres from the central cut end of sciatic nerve (of young rabbit) cut 10 days before death. (Cajal.)

A, fibres showing down-growth of axis-cylinders (*b*) which are invested by flattened nucleated cells; *a*, intact part still myelinated. B, a fibre, the axis-cylinder of which has not grown down with the rest, but which shows various degenerative appearances, such as buds from the axis-cylinder and at *d*, a separation of the fibrils.

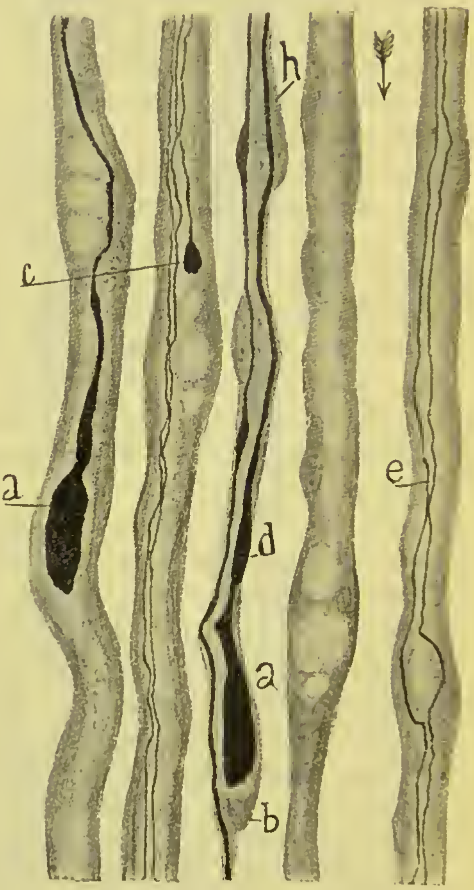

Fig. 226.—From the distal end of a nerve cut 78 days before death. (Cajal.)

a, *c*, enlarged growing ends of axis-cylinder sprouts which have grown down from the central cut end into the old sheaths of the cut nerve-fibres (myelin drops are still visible within the sheaths). The middle fibres (*h*) are interstitial (not in old sheaths). they show a new formation of a nucleated sheath. The fibre *d* has an enlarged end, *a*, with sheath *b*; *e*, very fine fibres within an old sheath; to the left of it, an old sheath without new fibres.

method, and are thus differentiated from the surrounding normal medullated nerves.

NEUROGLIA.

In the brain and spinal cord the nerve-cells and nerve-fibres are supported by a peculiar tissue which has been termed the *neuroglia.* It is composed of cells and fibres, the latter being prolonged from and through the cells. Of the fibres some are radially disposed. These start partly from the lining layer of the central canal of the spinal cord and the ventricles of the brain, where they are originally if not permanently continuous with the ciliated epithelium cells lining these cavities. They course in a radial direction, slightly diverging as they proceed, and constantly branching, towards the surface of the organ, where they end in enlargements attached to the pia mater. Radial neuroglia cells and fibres are seen in the embryo before the nervous elements are fully developed (fig. 227); when first distinct they are termed *spongioblasts* (His.).

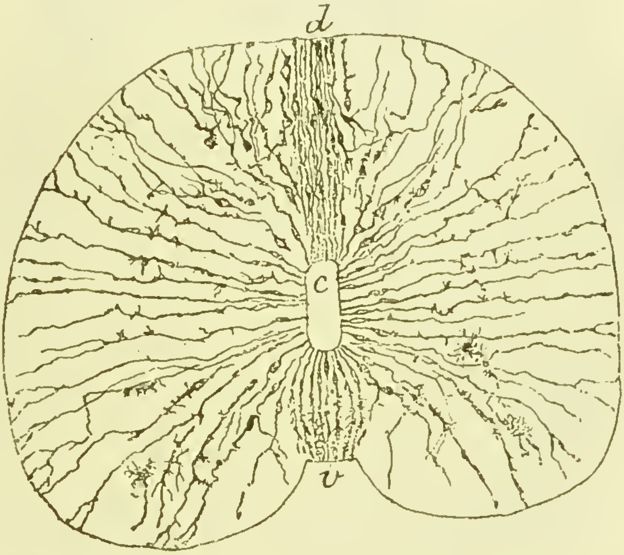

Fig. 227.—Section of spinal cord of embryo chick, showing neuroglia fibres prolonged from the epithelium of the central canal. (Cajal.)

d, dorsal; *v*, ventral surface; *c*, central canal from which the neuroglia cells and fibres are seen to radiate to the periphery of the cord. Some detached neuroglia cells are also represented.

Neuroglia-fibres are contained within prolongations or cell-processes of branching neuroglia-cells (*glia-cells*). The cells are stellate in shape (fig. 229), and their fine processes pass as neuroglia-fibres between the nerve-cells and nerve-fibres, which they aid in supporting (fig. 228). There appear to be two kinds of these neuroglia-cells differing from one another in the character of their processes (Andriezen). In the one kind the processes branch repeatedly (*arborescent cells*); in the other kind they remain unbranched from their origin in the cell-body to their termination (*spider-cells*).

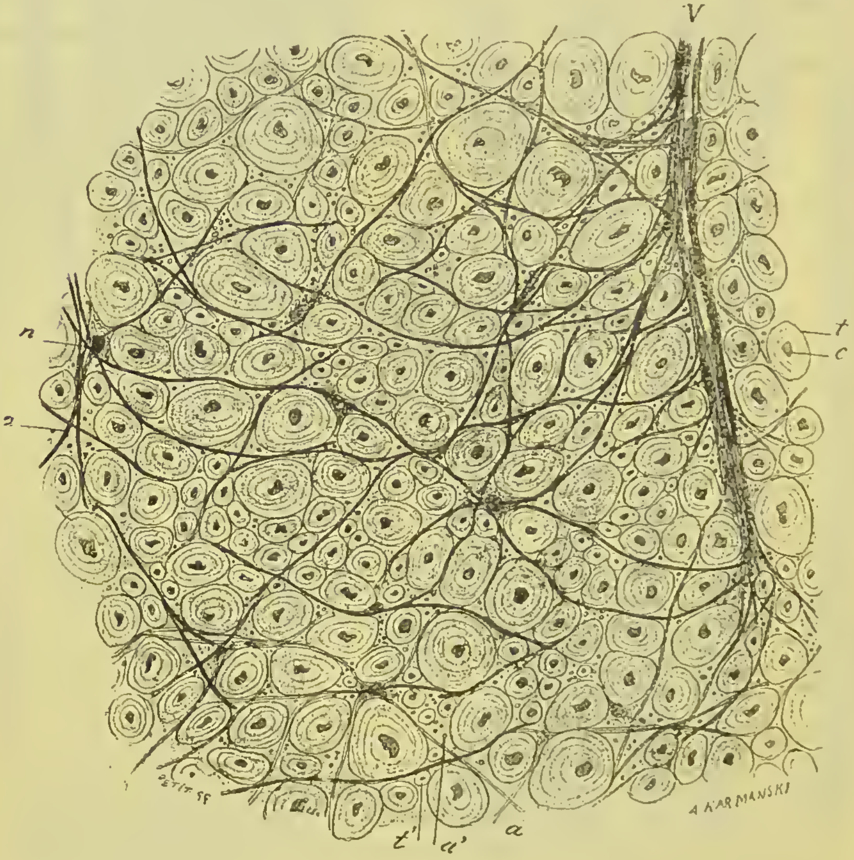

FIG. 228.—TRANSVERSE SECTION OF WHITE MATTER OF SPINAL CORD, SHOWING NERVE FIBRES CUT ACROSS AND NEUROGLIA FIBRES AMONGST THEM. (Ranvier.)

t, a medullary nerve fibre; *c*, its axis-cylinder; *t'*, a small fibre; *n*, neuroglia cell-body; *a*, *a*, neuroglia fibres; *a'*, others cut across.

Some authorities believe that the fibres of the neuroglia are inter- not intra-cellular, although it is admitted by all that they are formed originally by the neuroglia-cells.

DEVELOPMENT OF NERVE-CELLS AND NERVE-FIBRES.

All nerve-cells in the body are developed from the cells of the neural groove and neural crest of the early embryo; the neural groove closing to form the neural canal (fig. 230), the cells of which form the spinal cord and brain, and the neural crest giving off at intervals sprouts which become the germs of the spinal ganglia. The cells which line the neural canal are at first all long columnar cells, but amongst these, and probably produced by cell-division from some of these (fig. 231, *g*), rounded cells (*neuroblasts*) make their appearance, the remaining elongated cells forming the *spongioblasts*. Soon from each neuroblast a process begins to grow out (fig. 231, *n*, and fig. 232). This is the axon, and it is soon characterised by an enlarged extremity (*incremental cone*) (fig. 233, *h*, *h*; fig. 234, B, *c*). As it grows, it may emerge from the antero-lateral region of the canal and become the axis-cylinder of a *motor nerve* or *anterior root-fibre*. The dendrons of the cell appear somewhat later than the axon. The axis-cylinder processes of some of the neuroblasts remain within the nerve-centre, and are developed into commissural, association, and intercentral fibres. Harrison has directly observed the outgrowth of the axon processes of the neuroblasts of the amphibian larva in isolated neuroblasts examined in serum under the microscope. They can also be seen growing from the ends of the developing nerve-fibres in the tail of the tadpole.

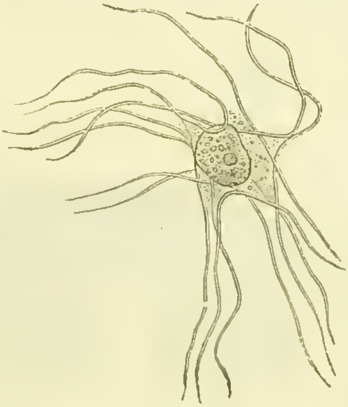

FIG. 229.—NEUROGLIA CELL FROM SPINAL CORD. (Ranvier.)
Isolated after maceration in 33 p.c. alcohol.

The sprouts from the neural crest contain the neuroblasts from which the posterior root-fibres are developed. Axons grow out from these neuroblasts in two directions, so that the cells become bipolar (fig. 235). One set of processes, forming the posterior root-fibres, grow into the dorsal portion of the spinal cord and ramify in the developing grey matter; the other set, containing the afferent fibres of the spinal nerves, grow towards the developing ventral roots, and eventually

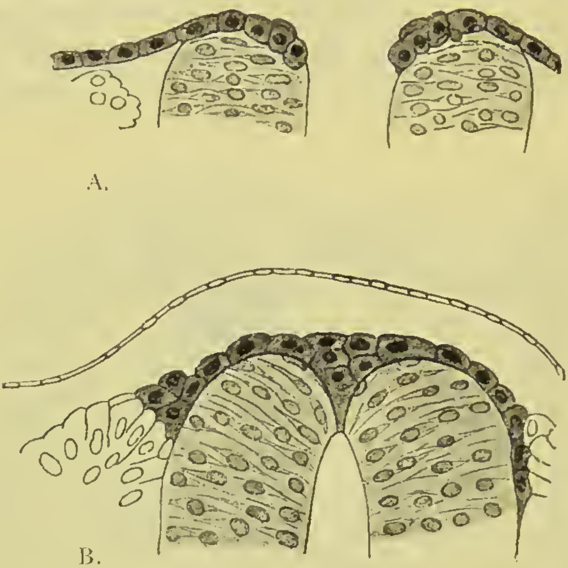

Fig. 230.—Closure of neural canal of human embryo, showing the cells of the neural crest becoming separated to form the germs of the spinal ganglia. (v. Lenhossék.)

A, canal still open; B, canal closed.

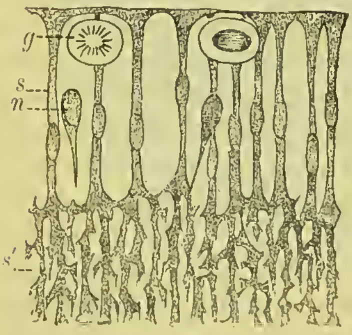

Fig. 231.

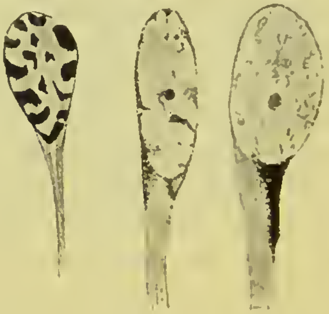

Fig. 232.

Fig. 231.—Section of neural epithelium of early embryo. (His.)

Highly magnified view of part of a section, at the time of the first differentiation of the neuroblasts, showing s', spongework formed of the outer ends of columnar epithelium cells, s; g, rounded "germinal cells" in process of division (probably to form neuroblasts); n, a neuroblast.

Fig. 232.—Neuroblasts from a pig-embryo, showing three stages of development. (Gurwitsch, after Scott.) Highly magnified.

mingle with them to form the mixed nerves. As development proceeds, the bipolar ganglion cells become gradually transformed in most vertebrates, by a shifting of the two axons, into unipolar cells (fig. 235, *h*, *i*, *j*; fig. 236); but in some fishes the cells remain permanently bipolar (fig. 206). This is also the case with the ganglion-cells of the eighth cranial nerve (ganglion of Scarpa and ganglion of the cochlea).

The ganglia on the sympathetic and on other peripheral nerves are developed from small masses of neuroblast cells which have wandered along the course of the out-growing nerve-fibres, and give origin to axons and dendrons much in the same way as do the neuroblasts within the central nervous system.

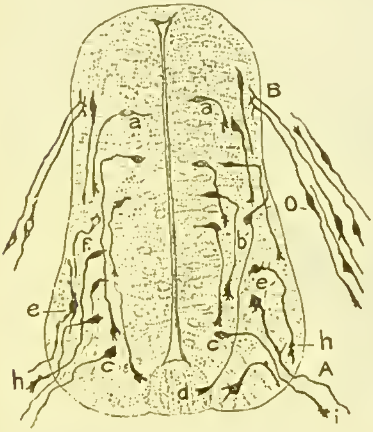

FIG. 233.

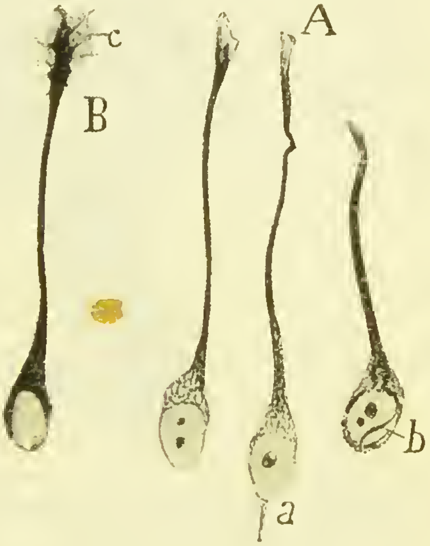

FIG. 234.

FIG. 233.—SECTION OF SPINAL CORD OF CHICK OF THIRD DAY OF INCUBATION. (Cajal.)

A, anterior root-fibres formed by outgrowths of motor neuroblasts, *c*, *e*; B, posterior root-fibres formed by ingrowths of bipolar sensory neuroblasts, *o*, in ganglion rudiment; *a*, early neuroblasts; *b*, neuroblast giving rise to a commissural nerve-fibre, *d*; *h*, *i*, enlarged ends of growing axons; *e*, *e*, neuroblasts of which the dendrons are beginning to appear.

FIG. 234.—NEUROBLASTS FROM THE SPINAL CORD OF A THIRD-DAY CHICK EMBRYO. (Cajal.)

A, three neuroblasts, stained by Cajal's reduced silver method, showing a network of neuro-fibrils in the cell-body; *a*, a bipolar cell. B, a neuroblast stained by the method of Golgi, showing the incremental cone, *c*.

The manner in which the medullary sheath and neurolemma of the nerve-fibres are formed is not fully understood. It is probable that the medullary substance at any rate is formed by the axis-cylinder itself, although the neurolemma with its nuclei may be derived from cells which have either wandered out from the neural ectoderm or are of mesodermic origin.

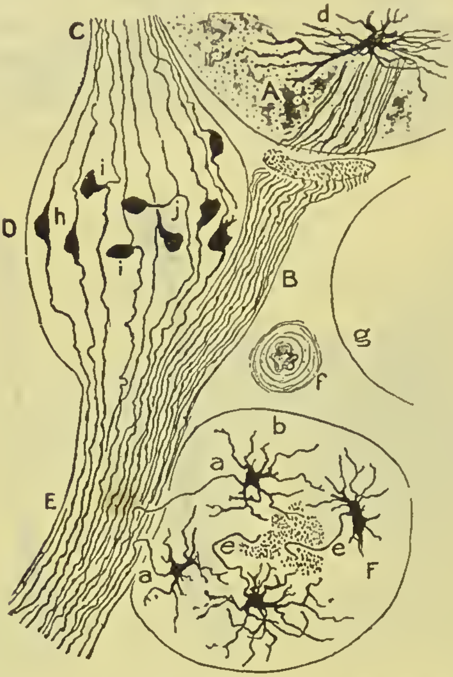

Fig. 235.—Spinal and sympathetic ganglia and part of spinal cord of chick of seventeenth day of incubation. (Cajal.)

A, antero-lateral part of spinal cord with *d*, a motor nerve-cell; the fibres of the anterior root are seen emerging and passing to B (the connection appears interrupted in the section); C, posterior root formed of fibres which have grown from the ganglion-cells in D, spinal ganglion; E, mixed spinal nerve; F, sympathetic ganglion; *a*, *a*, axons of sympathetic cells, passing to join the spinal nerve; *b*, dendrons of these cells; *e*, axons passing to the sympathetic cord; *h*, cells of spinal ganglion still bipolar; *i*, *i*, bipolar cells becoming transformed into unipolar; *e*, unipolar cell with T-junction; *f*, section of an artery; *g*, body of vertebra.

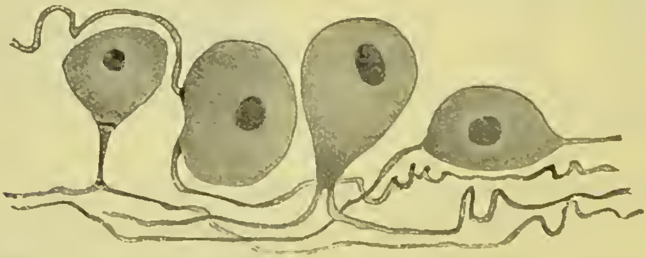

Fig. 236.—Spinal ganglion-cells showing transitions from bipolar to unipolar condition. (Holmgren.)

The neuroglia-cells appear to be developed from ectoderm cells (spongioblasts) of the wall of the neural canal, which, in place of giving off axon and dendrons like the neuroblasts, send out a number of fine processes in all directions from the cell to form the fibres of the neuroglia. It is held by some authorities that the neuroglia has a double origin, some of the cells with unbranched processes being developed from ectoderm and the others from mesoderm.

Some neurologists are of opinion that the nerve-fibres do not grow out from single nerve-cells in the manner above described, but are formed of chains of cells which emerge from the neural ectoderm or from the ganglion-rudiments, and join end to end into a syncytium, which gradually lengthens out into the nerve-fibre, the nuclei of the syncytium becoming the nuclei of the neurolemma, and the protoplasm of the syncytium becoming differentiated into axis-cylinder, medullary sheath, and neurolemma as development advances. Others, whilst agreeing that the axis-cylinders grow out as cell processes from the neuroblasts of the neural canal and ganglia, describe those out-growing processes as surrounded by other neural ectoderm cells—*lemmal cells*—which accompany them in their progress through the tissues, multiplying as they proceed, and forming eventually the nucleated sheath of the medullated nerve.

LESSON XIX.

MODES OF TERMINATION OF NERVE-FIBRES.

1. Shell out a Pacinian corpuscle from a piece of cat's mesentery, which may either be fresh or may have been kept for two or three days in $\frac{1}{20}$ per cent. chromic acid or in 5 per cent. formol. Clear it as much as possible of adhering fat, but be careful not to prick or otherwise injure the corpuscle itself. Mount in water or saline with a thick hair to prevent crushing with the cover-glass. Sketch the corpuscle under a low power, and afterwards draw under a high power the part of the core where the nerve enters and the part where it terminates. Notice the fibrous structure of the lamellar tunics of the corpuscle and the oval nuclei belonging to flattened epithelioid cells which cover the tunics. The distinct lines, which when seen in the fresh corpuscles are generally taken for the tunics, are really the optical sections of these flattened cells.

2. Pacinian corpuscles may often be observed in sections of skin in the subcutaneous tissue ; tactile corpuscles may be seen in the papillæ of the palmar surface of the hand and fingers.

3. Dissect off a small portion of conjunctiva from the eye of a calf or other animal. Spread it out on a slide with the under surface uppermost, and place upon it a drop of 1 per 1000 methylene blue solution. Watch the preparation with a low power until the nerve-fibres come into view, then cover and trace them with the high power. They will be seen to end in elongated end-bulbs.

Somewhat similar endings can be shown in the same manner in a piece of parietal peritoneum stripped off and laid out flat upon a slide and mounted in methylene blue solution.

4. Study the corpuscles of Grandry and of Herbst in sections of the skin covering the duck's bill.

5. Mount in dilute glycerine sections of a rabbit's cornea which has been stained with chloride of gold by Klein's method. Notice the arrangement in plexuses of the darkly-stained nerve-fibres and fibrils, (1) in the connective-tissue substance, (2) under the epithelium, and (3) between the epithelial cells. Make one or two sketches showing the arrangement of the fibrils.

6. Spread out a small piece of muscle which has been stained with chloride of gold by Löwit's method, or with hæmatoxylin by Sihler's method, and examine it with a low power to find the nerve-fibres crossing the muscular fibres and distributed to them. Occasionally the nerve-fibres which end in the muscle-spindles may be observed.

The pieces of muscle are advantageously thinned out for observation by pressure upon the cover-glass. Search thoroughly for the close terminal ramifications (end plates) of the axis-cylinders immediately within the sarcolemma.

These nerve-endings as well as others elsewhere can also be displayed in preparations made by Ehrlich's, Golgi's, or Cajal's methods (see Appendix).

Modes of ending of sensory nerve-fibres.—Nerve-fibres which are distributed to sensory parts end either in *special organs* or in free *terminal ramifications*, these last being usually in epithelia. Within the special organs the actual nerve-ending is also generally ramified.

Nerve-endings in special connective-tissue organs.—Three chief kinds of these special organs are usually described, represented in man by *Pacinian corpuscles*, *tactile corpuscles*, and *end-bulbs.* The type is the same in all: a lamellated connective-tissue *capsule* inclosing a *core* of a soft material which appears to be composed of nucleated protoplasmic cells; the capsule being an expansion of the perineurium, and the core an expansion of the endoneurium of the nerve. Within the core the axis-cylinder terminates either simply or by a more or less complex arborescence. The variations which occur are chiefly due to the complexity of the capsule, which is simplest in the end-bulbs and most complex in the Pacinian corpuscles. In the **tactile corpuscles** and **end-bulbs** the connective-tissue sheath of the medullated fibre expands to

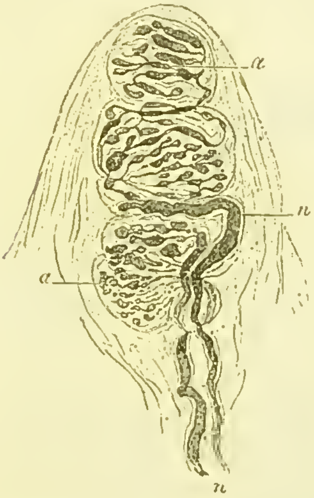

FIG. 237.

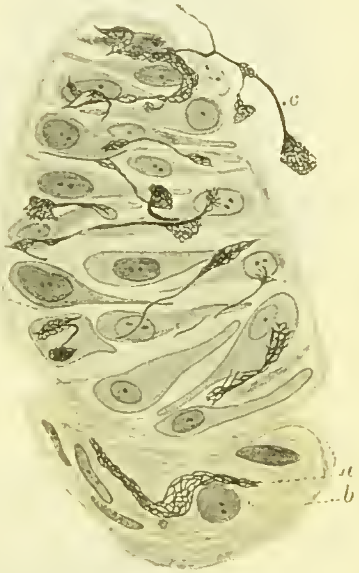

FIG. 238.

FIG. 237.—TACTILE CORPUSCLE WITHIN A PAPILLA OF THE SKIN OF THE HAND, STAINED WITH CHLORIDE OF GOLD. (Ranvier.)

n, two nerve-fibres passing to the corpuscle; *a*, *a*, varicose ramifications of the axis-cylinders within the corpuscle.

FIG. 238.—SECTION OF A TACTILE CORPUSCLE, SHOWING THE CELLS COMPOSING THE CORE AND THE RAMIFICATIONS OF THE AXIS-CYLINDER AMONGST THEM, ENDING IN FIBRILLATED ENLARGEMENTS. (Van de Velde.)

a, axis-cylinder; *b*, capsule of corpuscle; *c*, a nerve-termination outside the corpuscle.

form a bulbous enlargement, which is cylindrical or spheroidal in the end-bulbs and ellipsoidal in the tactile corpuscles. In both kinds of

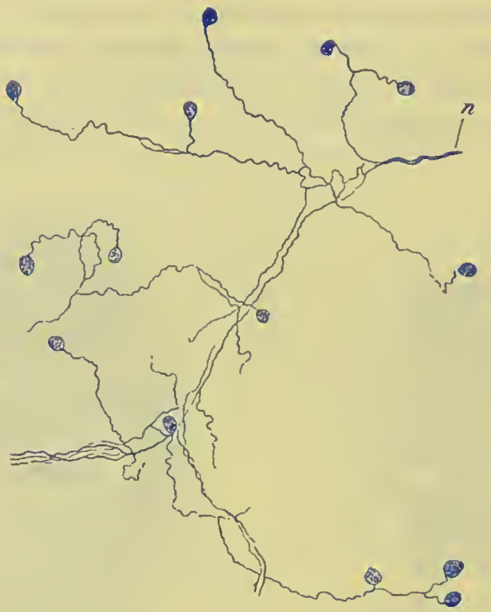

FIG. 239.—END-BULBS AT THE TERMINATIONS OF NERVES IN THE HUMAN CONJUNCTIVA, AS SEEN WITH A LENS. (Longworth.)

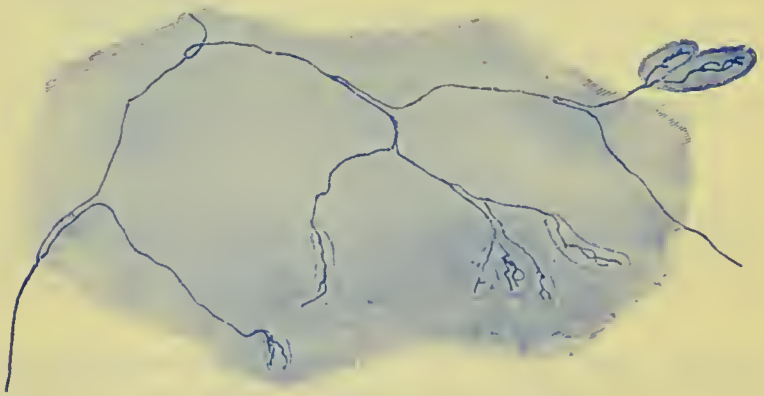

FIG. 240.—A MEDULLATED FIBRE TERMINATING IN SEVERAL END-BULBS IN THE HUMAN PERITONEUM. (A. S. Dogiel.) Methylene blue preparation. Low power.

end-organ as the nerve-fibre enters (which in the tactile corpuscle only happens when it has reached the distal part, after having wound spirally once or twice round the corpuscles) it loses its sheath and is prolonged as an axis-cylinder only; this generally ramifies and its branches terminate after either a straight or a convoluted course within the organ; but it sometimes remains almost unbranched (see figs. 237 to 242). Tactile corpuscles occur in some of the papillæ of the skin of the hand and foot, in sections of which they can be studied (see fig. 332, p. 262). End-bulbs are found in the conjunctiva of the eye, where in most animals they have a cylindrical or oblong shape, but in man they are spheroidal (fig. 239). They have also been found in papillæ of the lips and tongue, in serous membranes, in tendons and aponeuroses, and in the epineurium of the nerve-trunks; and somewhat similar sensory end-organs (*genital corpuscles*) also occur in the integument of the external genital organs of both sexes (fig. 243). Similar bodies of larger size are also met with in the neighbourhood of the joints (*articular corpuscles*). In the skin

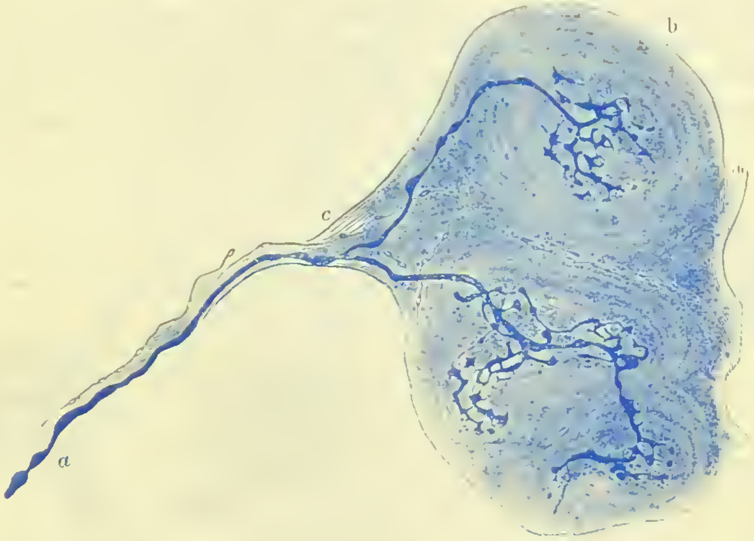

FIG. 241.—END-BULBS FROM THE HUMAN PERITONEUM. (Dogiel.) More highly magnified. Methylene blue preparation.

a, medullated fibre; *b*, nucleated lamellated capsule of end-bulb; *c*, non-medullated fibres, probably destined for the capillaries which surround the end-bulbs.

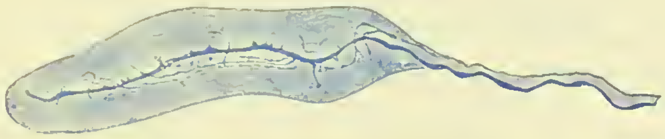

FIG. 242.—END-BULB FROM THE CENTRAL TENDON OF THE DIAPHRAGM OF THE DOG. (Dogiel.) Showing besides the main medullated fibre terminating by an arborescence within the core, a second very fine medullated fibre, forming a more delicate arborescence around the ending of the main fibre in the outer part of the core. Methylene blue preparation.

covering the bills of certain birds (*e.g.* duck), a simple form of end-organ (*corpuscle of Grandry*, fig. 244) occurs, consisting of two or more cells arranged in rows within a capsule, with the axis-cylinder terminating in flattened expansions (*tactile disks*) between the cells.

The **Pacinian corpuscles** are larger, and have a more complex structure, than the tactile corpuscles and end-bulbs (fig. 245). They are composed of a number of concentric coats arranged like the layers of an onion, and inclosing the prolonged end of a nerve-fibre. A single medullated nerve-fibre goes to each Pacinian corpuscle, encircled by a prolongation of the perineurium (*sheath of Henle*), and within this by endoneurium; when it reaches the corpuscle, of which it appears to form the stalk, the lamellæ of the perineurium expand into the tunics of the capsule. The nerve passes on, piercing the tunics, surrounded by endoneurium, and still provided with medullary sheath, to reach the central part of the corpuscle. Here the endoneurium is prolonged to form a core of cylindrical shape, along the middle of which the nerve-fibre, now deprived of its medullary sheath and neurolemma, passes in a straight course as a simple axis-cylinder (figs. 245, *n*′; 247, *c.f*) to terminate at the farther end of the core, either in an arborisation or in a bulbous enlargement. In its course through the core it may give off lateral ramifications, which penetrate to all parts of the core, and themselves end in fine branches.

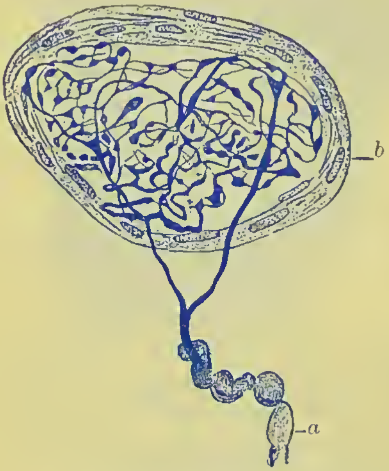

FIG. 243.—END-BULB FROM THE GLANS PENIS, SHOWING ENDING OF AXIS-CYLINDER. Methylene blue preparation. (Dogiel.)

a, medullated nerve-fibre; *b*, sheath of end-bulb.

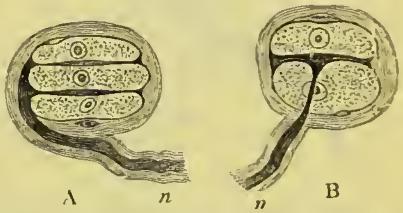

FIG. 244.—GRANDRY CORPUSCLES FROM THE DUCK'S TONGUE. (Izquierdo.)

A, composed of three cells, with two interposed disks, into which the axis-cylinder of the nerve, *n*, is observed to pass; in B there is but one tactile disk inclosed between two tactile cells.

Besides the medullated fibre, which is always very conspicuous, it has been shown that both the Pacinian and Herbst corpuscles receive in addition a fine non-medullated nerve-fibre, which arborises over the outer surface of the core. A similar arrangement also obtains in Grandry's corpuscles, where the tactile cells are surrounded with such an arborisation (Dogiel and others).

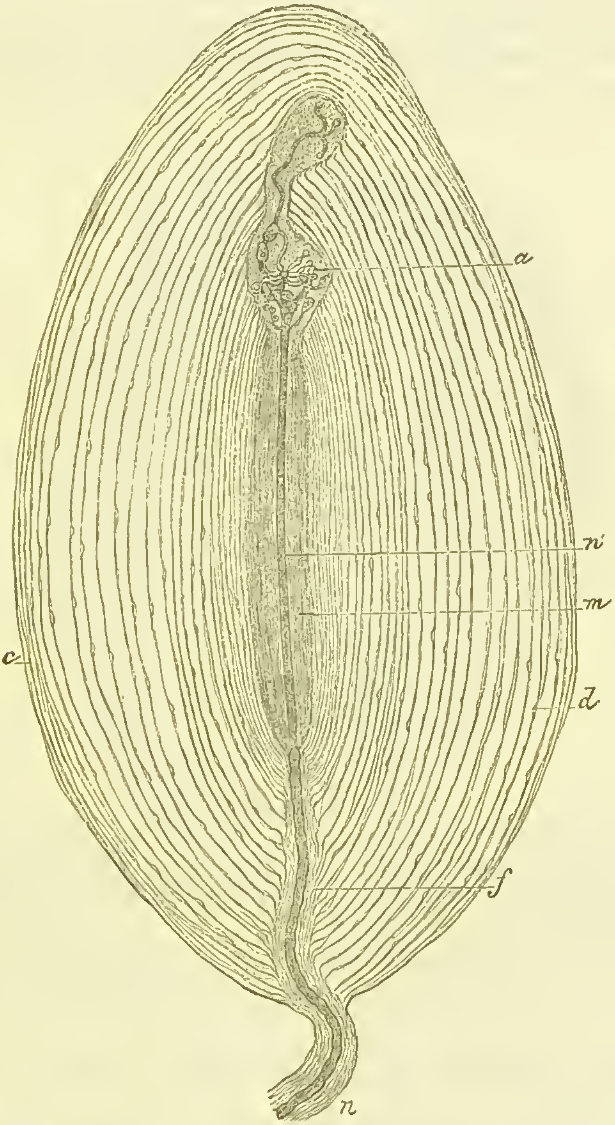

FIG. 245.—MAGNIFIED VIEW OF A PACINIAN BODY FROM THE CAT'S MESENTERY. (Ranvier.)

n, stalk of corpuscle with nerve-fibre, inclosed in sheath of Henle, passing to the corpuscle; *n'*, its continuation through the core, *m*, as axis-cylinder only; *a*, its terminal arborisation; *c*, *d*, sections of epithelioid cells of tunics, often mistaken for the tunics themselves; *f*, channel through the tunics which expands into the core of the corpuscle.

The tunics of the capsules are composed of connective tissue, the fibres of which for the most part run circularly. They are covered on both surfaces with a layer of flattened epithelioid cells (fig. 248), and here and there cleft-like lymph-spaces can be seen between them like those between the layers of the perineurium.

Pacinian corpuscles occur in many parts, *e.g.* in the deeper layers of the skin of the hands and feet, in the periosteum of some bones, in the neighbourhood of tendons and ligaments, in the connective tissue at the back of the abdomen, and (in the cat) very numerously in the mesentery, where they are most easily got for observation.

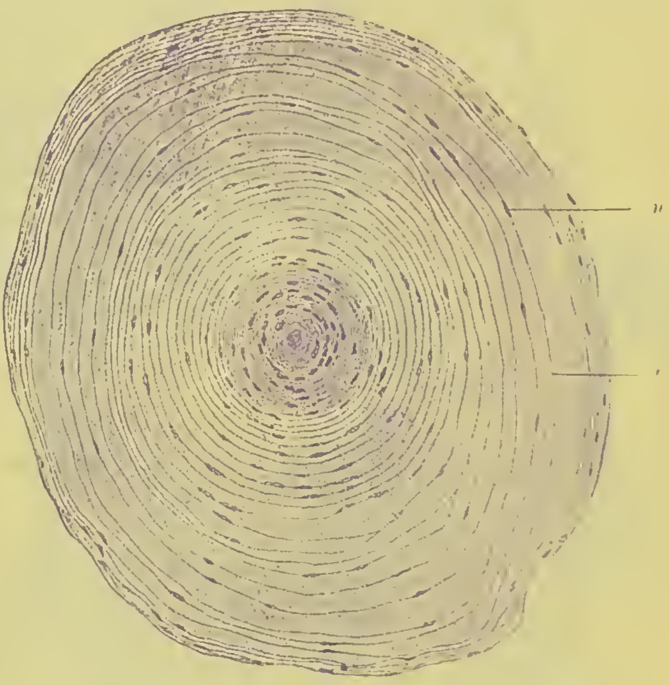

FIG. 246.—SECTION OF PACINIAN CORPUSCLE. (Szymonowicz.)

e, one of the layers of epithelioid cells; *n*, nucleus of epithelioid cell. It is seen that the tunics are very closely packed around the core, in the middle of which the axial-fibre is cut across.

A simple form of Pacinian corpuscle with fewer tunics and a core formed of regularly arranged cells occurs in birds (*corpuscles of Herbst*, fig. 249).

Although most of the nerve-endings in connective-tissue structures are enclosed within lamellated capsules, nerves are found to end in some situations in arborisations between the bundles of connective-tissue fibres. This has been shown by Dogiel to occur in intermuscular connective-tissue septa (fig. 250); and in serous membranes (fig. 251);

in the latter such arborisations may be quite superficial and placed just below the endothelium.

Organs of Ruffini.—These, which resemble long cylindrical end-bulbs, are composed of connective-tissue bundles, within which the axis-cylinders of the nerves ramify, and end in flattened expansions. They occur commonly in the subcutaneous tissue of the human finger (figs. 252, 253). Other end-bulb-like organs, spheroidal, oval, or cylindrical in form, have been described by Ruffini under the name of Golgi-Mazzoni corpuscles (fig. 254); they appear to be varieties of the ordinary end-bulb of W. Krause. They occur in tendons and in the subcutaneous tissue of the pulp of the finger.

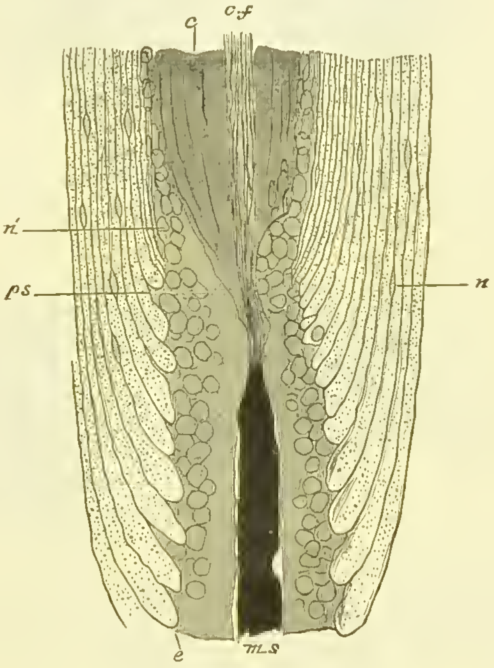

Fig. 247.—Part of Pacinian body, showing the nerve-fibre entering the core. From an osmic acid preparation.

ms, entering nerve-fibre, the medullary sheath of which is stained darkly, and ends abruptly at the core, *c*; *ps*, prolongation of primitive sheath or neurolemma passing towards the outer part of the core; *cf*, axis-cylinder passing through the core as the central fibre; *e*, some of the inner tunics of the corpuscle, enlarged where they abut against the canal through which the nerve-fibre passes—the dots within them are sections of the fibres of which they are composed; *n*, nuclei of the tunics; *n′*, nuclei of the endoneurium-cells, continued by others in the outer part of the core.

Organs of Golgi.—A special mode of nerve-ending is met with in many tendons, near the points of attachment of the muscular fibres. The tendon-bundles become somewhat enlarged and split into a

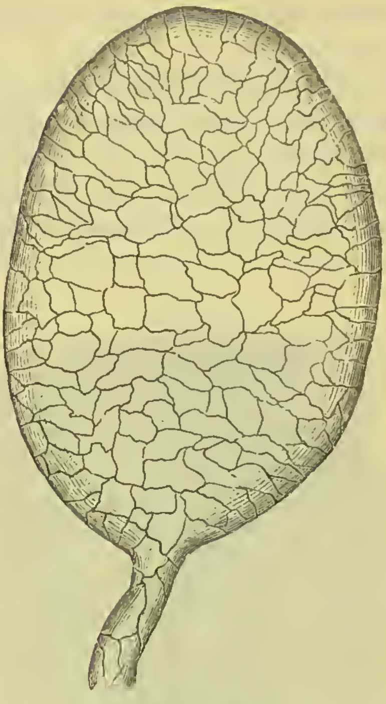

FIG. 248.—PACINIAN CORPUSCLE FROM THE CAT, STAINED WITH SILVER NITRATE. (Drawn by G. C. Henderson.)

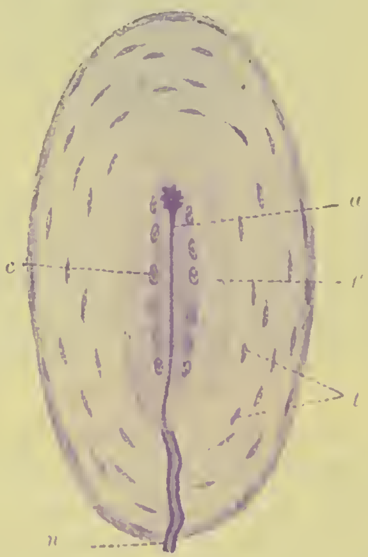

FIG. 249.—HERBST CORPUSCLE OF DUCK. (Sobotta.) × 380.

n, medullated nerve-fibre ; *a*, its axis-cylinder, terminating in an enlargement at end of core ; *c*, nuclei of cells of core ; *t*, nuclei of cells of outer tunics ; *t'*, inner tunics.

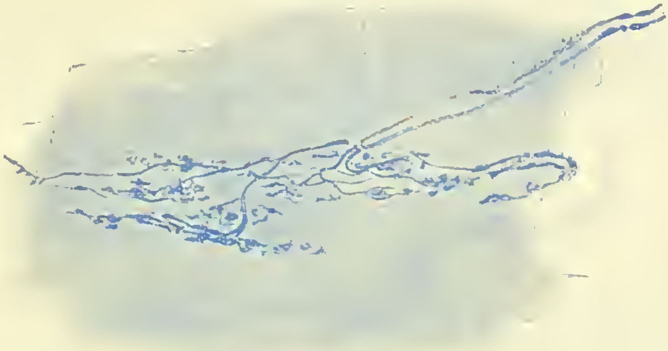

FIG. 250.—TERMINAL ARBORISATION FROM THE INTERMUSCULAR CONNECTIVE TISSUE OF THE RECTUS ABDOMINIS OF THE RABBIT. METHYLENE BLUE PREPARATION. (Dogiel.)

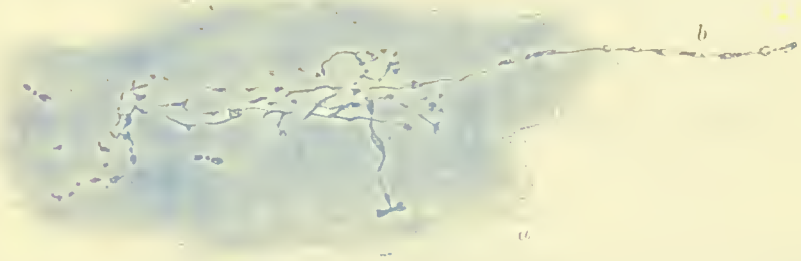

FIG. 251.—TERMINAL ARBORISATION FROM THE SUPERFICIAL LAYER OF THE PERITONEUM OF THE RABBIT. METHYLENE BLUE PREPARATION. (Dogiel.)

a, medullated fibre ; *b*, fibre connecting the arborisation with another one not here represented.

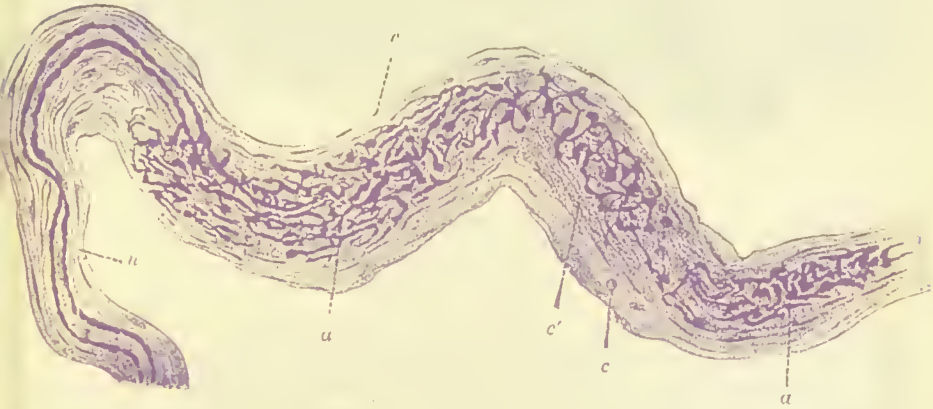

FIG. 252.—AN ORGAN OF RUFFINI FROM THE SUBCUTANEOUS TISSUE. (Ruffini.)

n, entering nerve-fibres ; *a*, *a*, ending of their axons ; *c*, *c*, capsule of organ ; *c′*, core.

number of smaller fasciculi, and the nerve-fibres—one, two, or even more in number—pass to the enlarged part, and penetrating between the fasciculi of the tendon lose their medullary sheaths, while the axis-cylinders end in a terminal arborisation, beset with irregular varicosities. The structure (figs. 255, 256) is enclosed within a fibrous capsule continuous with the areolar tissue covering the bundles of the tendon; and between the capsule and the organ proper is a lymph-space, similar to that which is found in the muscle-spindle (see p. 203).

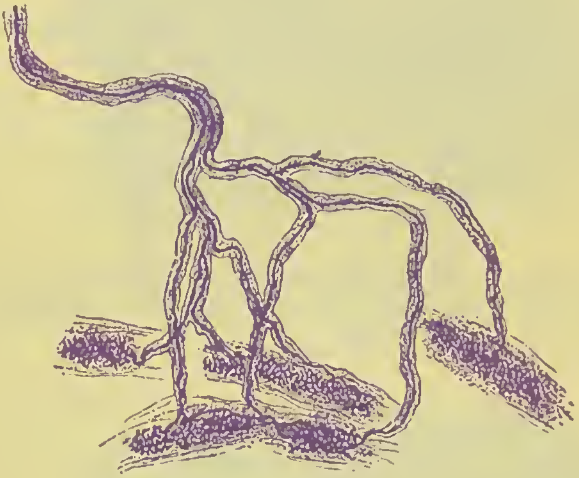

FIG. 253.—A NERVE-FIBRE IS SHOWN DIVIDING INTO SEVEN SECONDARY FIBRES TO WHICH ARE ATTACHED FIVE ORGANS OF RUFFINI. (Barker, after Ruffini.)

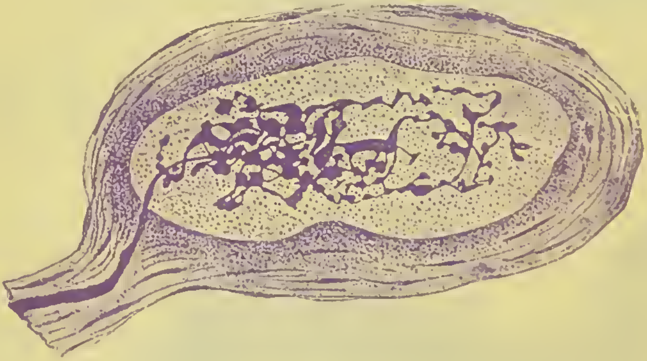

FIG. 254.—ORGAN OF GOLGI-MAZZONI FROM SUBCUTANEOUS TISSUE. (Ruffini.) The organ resembles an end-bulb in general structure.

Free nerve-endings. — When sensory nerve-fibres terminate in epithelium, they generally branch once or twice in the subepithelial connective tissue on nearing their termination. The sheaths of the fibres then successively become lost, first the connective tissue or

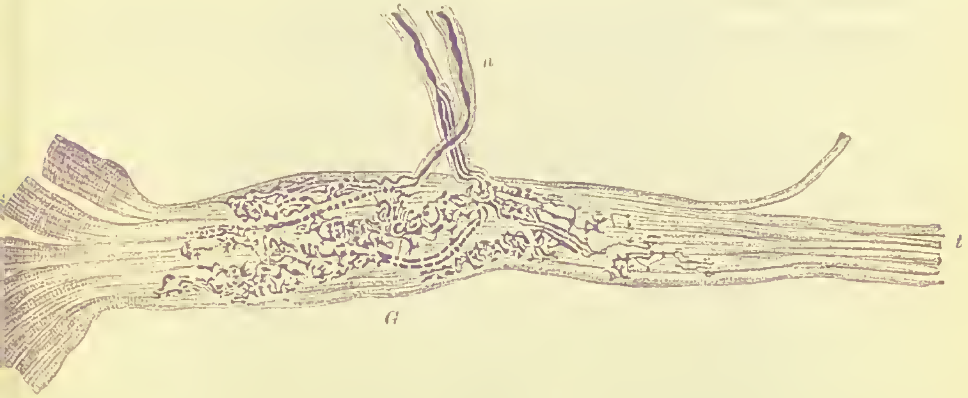

Fig. 255.—Organ of Golgi from the human tendo Achillis. Chloride of gold preparation. (Ciaccio.)

m, muscular fibres ; *t*, tendon-bundles ; *G*, Golgi's organ ; *n*, two nerve-fibres passing to it.

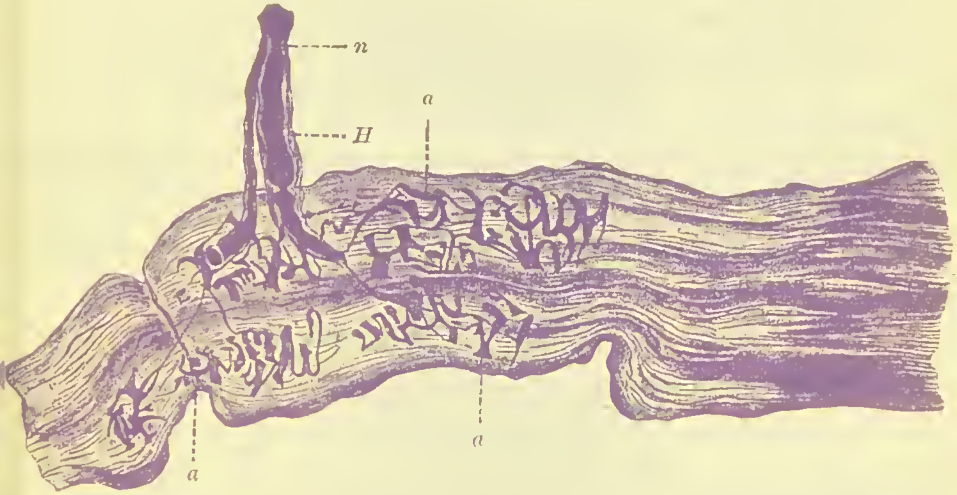

Fig. 256.—Organ of Golgi, more highly magnified. (Ciaccio.)

n, entering nerve-fibre ; *H*, its sheath of Henle ; *a*, *a*, ramification of axis-cylinders between the tendon-bundles.

perineural sheath, then the medullary sheath, and lastly the neurolemma, the axis-cylinder being alone continued as a bundle of primitive fibrils. This branches, and with the ramifications of the axis-cylinders of neighbouring nerve-fibres forms a primary plexus. From the primary plexus smaller branches come off, and these form a secondary plexus nearer the surface, generally immediately under the epithelium if the ending is in a membrane covered by that tissue. Finally, from the secondary plexus nerve-fibres proceed and form terminal ramifications amongst the tissue cells (fig. 257, *p*, *b*), the actual ending being generally in free varicose fibrils (*b*). This mode of ending is characteristically seen in the cornea of the eye, but can also be rendered evident in other epithelia (fig. 258).

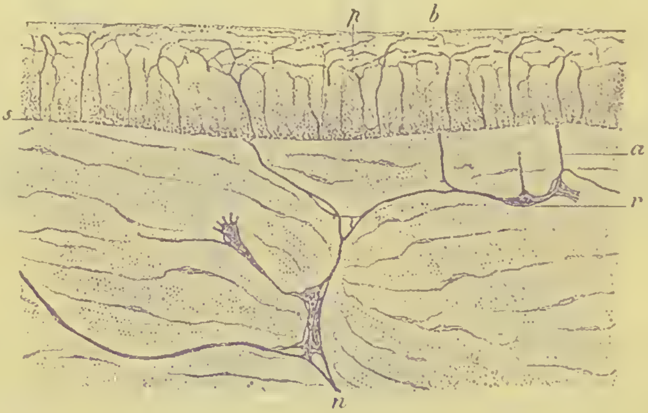

FIG. 257.—VERTICAL SECTION OF CORNEA STAINED WITH CHLORIDE OF GOLD. (Ranvier.)

n, *r*, primary plexus in connective tissue of cornea ; *a*, branch passing to subepithelial plexus, *s* ; *p*, intra-epithelial plexus ; *b*, terminations of fibrils.

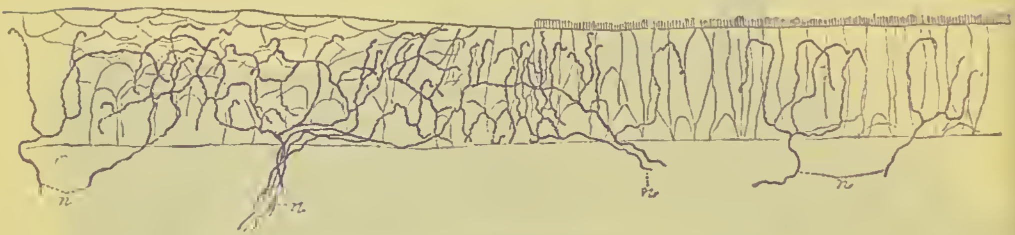

FIG. 258.—INTRA-EPITHELIAL NERVE-TERMINATIONS IN THE LARYNX. GOLGI METHOD. (G. Retzius.)

On the left the epithelium is stratified and on the right ciliated columnar. *n*, nerve-fibres in corium.

In some situations the nerve-fibrils within a stratified epithelium terminate in flattened or crescentic expansions which lie in the interstices of the deeper epithelium cells, to some of which they are applied. These expansions are known as *tactile disks*; they are characteristically developed in the skin of the pig's snout (fig. 259), and are also found in the outer root sheath of hairs and in the deeper parts of the epidermis in various parts. With appropriate treatment it may be shown that they consist of a fine network of neuro-fibrils.

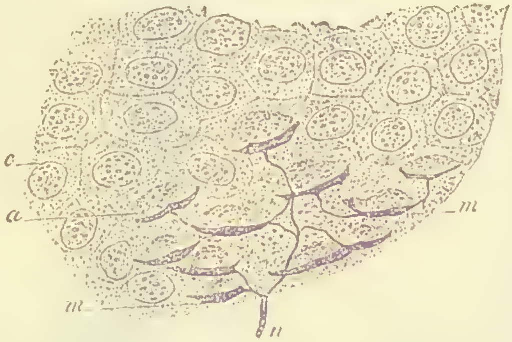

FIG. 259.—ENDING OF NERVE IN TACTILE DISKS IN THE PIG'S SNOUT. (Ranvier.)

n, medullated fibre; *m*, terminal disks or menisci; *c*, cells of the Malpighian layer of the epidermis; ***a***, somewhat modified cell to which a tactile disk is applied.

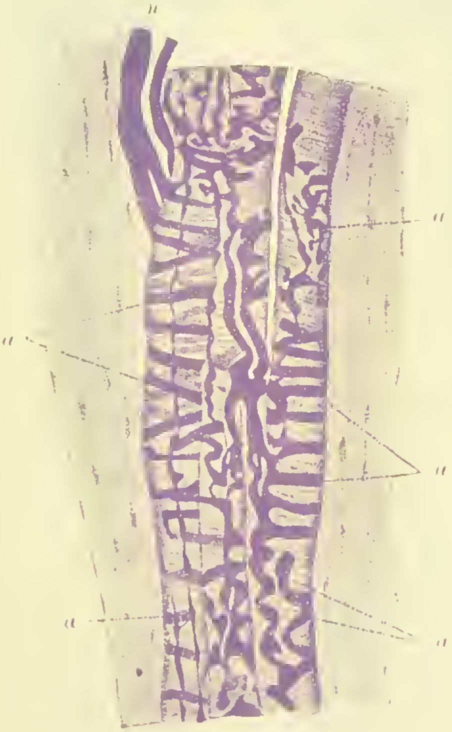

FIG. 260.—ENDING OF NERVE-FIBRES IN MUSCLE-SPINDLE. (Ruffini.)

Three intrafusal muscle-fibres are shown. *n*, nerve-fibres entering spindle; *a*, axis-cylinders terminating around and between the intrafusal fibres in ring-like, spiral, and irregularly ramified endings.

Sensory nerves of muscles.—The sensory nerves of muscles end in peculiar organs which were termed by Kühne *muscle-spindles.*

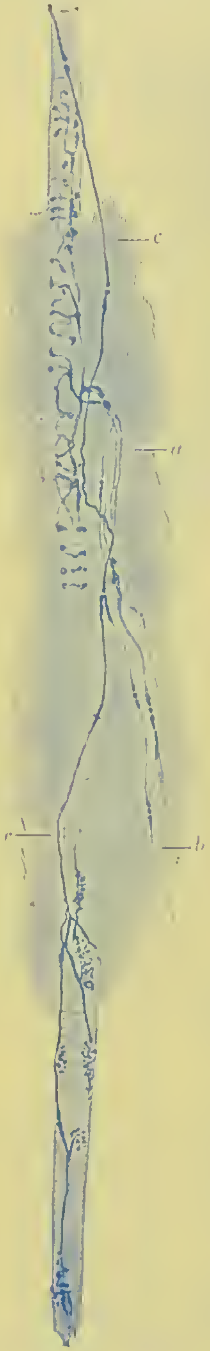

Fig. 261.

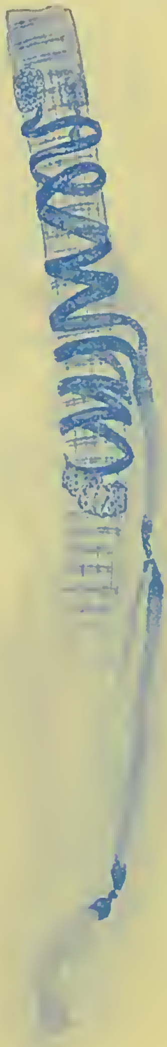

Fig. 262.

Fig. 261.—Nerve-endings upon the intrafusal muscle-fibres of a muscle-spindle of the rabbit; moderately magnified. Methylene blue preparation. (Dogiel.)

a, large medullated fibre coming off from "spindle" nerve and passing to end in an annulo-spiral termination on and between the intrafusal fibres; *b*, a fine medullated fibre coming off from the same stem and dividing. Its branches, *c*, pass towards the ends of the muscle-fibres and terminate in a number of small localised flower-spray-like arborisations.

Fig. 262.—An annulo-spiral ending of intrafusal fibre; highly magnified. Methylene blue preparation. (Dogiel.)

Their structure has recently been specially investigated by Ruffini, Huber, and Dogiel, and also by Sherrington, who has shown that the large medullated nerves which they receive (about three or four such fibres entering each spindle not far from its equator), are derived from the posterior root-ganglia.

The **muscle-spindle** is a fusiform body, from 0·75 to 4 mm. long, and from 0·08 to 0·2 mm. in diameter; it lies parallel with the general direction of the fibres of a muscle. It consists of a lamellated connective-tissue sheath externally, within which is a bundle (intrafusal bundle) of from two to twelve peculiar muscle-fibres. These form an axial mass with some connective tissue and the nerve-fibres; between this axial bundle and the sheath is a lymphatic periaxial space, bridged across by filaments of connective tissue. The intrafusal muscle-fibres are somewhat like embryonic fibres in appearance, being smaller than the ordinary fibres of the muscle and having a relatively large number of nuclei with surrounding protoplasm, as in the red variety of muscle. At the proximal end of the spindle they are usually only two or three in number, but they become cleft as they pass through it; at the distal end they may terminate in tendon-bundles. The nerve-fibres which pass to the spindle are mostly of large size; they divide after reaching

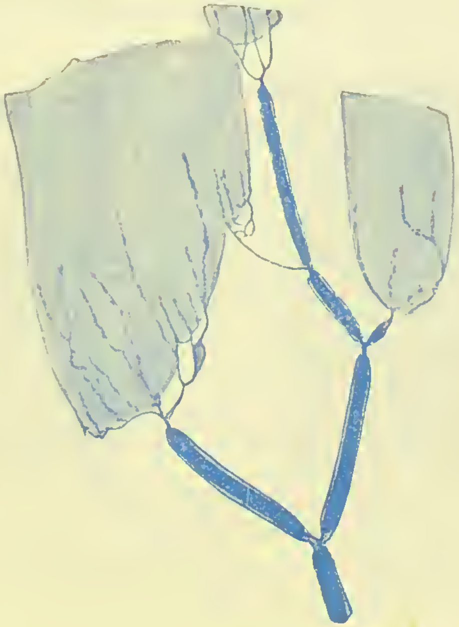

FIG. 263.—SENSORY NERVE TERMINATING IN ARBORISATIONS AROUND THE ENDS OF MUSCLE-FIBRES. (Ceccherelli.)

the intrafusal bundle, but retain their medullary sheath for a time, although eventually terminating as axis-cylinders merely, which wind in a spiral manner around the intrafusal muscle-fibres (figs. 260, 261, 262), which they clasp by flattened encircling branches (*annulo-spiral endings*). Other, much finer, medullated fibres also pass to the spindle and terminate in neighbouring parts of the intrafusal bundles in flower-like or plate-like expansions (fig. 261). According to some observers these fine fibres are prolonged from the annulo-spiral endings of the coarser fibres; but Dogiel states that they may run independently to the intrafusal bundle. No motor nerve-fibres appear to pass into the spindles, unless the fine fibres above mentioned are to be so regarded, nor do the muscle-fibres of the spindle undergo atrophy on section of the motor nerve-roots, as is the case eventually with the ordinary muscle-fibres. It is not uncommon to find two or three spindles close together or even inclosed in a common sheath. Muscle-spindles are few in number in the eye-muscles, and have not yet been found in the muscles of the tongue, but otherwise their occurrence is general.

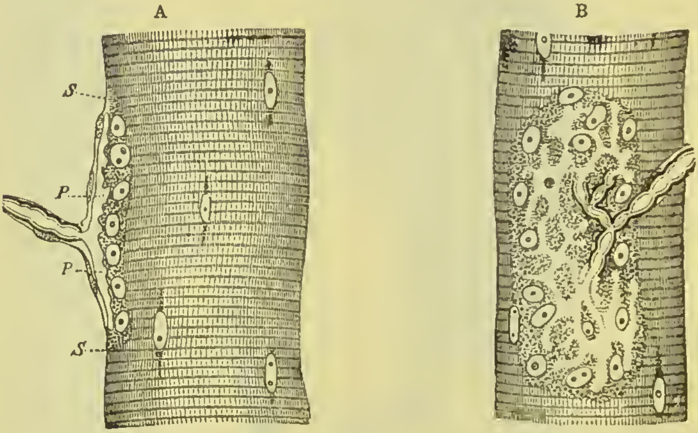

FIG. 264.—NERVE-ENDING IN MUSCULAR FIBRE OF A LIZARD (Lacerta viridis). (Kühne.)

A, end-plate seen edgeways; B, from the surface; *s*, *s*, sarcolemma; *p*, *p*, expansion of axis-cylinder. In B the expansion of the axis-cylinder appears as a clear network branching from the divisions of the medullated fibres.

In the frog both motor and sensory nerves may terminate in and between the same muscle-fibres, but at different parts of the fibre. It is not known whether the muscle-fibres of the spindles also receive motor nerves in mammals.

Another kind of ending of sensory fibres in muscle has been described by Ceccherelli, in the form of an arborisation of nerve-fibrils around the ends of the muscle-fibres which are inserted into tendon (fig. 263).

Ending of motor-nerves.—The motor-nerves to muscles terminate in fine ramifications of the axis-cylinder; in striated (voluntary) muscles the ramification is localised in special organs termed *motor end-organs*, or less correctly, *end-plates.*

In **voluntary muscle,** the nerves, which are always medullated, terminate, as just stated, in special end-organs (figs. 264 to 266). A medullated fibre will branch two or three times before ending, and then each branch passes straight to a muscular fibre. Having reached this, the neurolemma of the nerve-fibre is continued into the sarcolemma of the muscle, the medullary sheath stops short, and the axis-cylinder ends in a close terminal ramification with varicose expansions upon its branches. This ramification is embedded in a layer of granular nucleated protoplasm (*sole*) (fig. 266, *b*), probably a development of the sarcoplasm of the muscle. In some cases the ramification is restricted to a small portion of the muscular fibre, and forms with the granular bed a slight prominence (*eminence of Doyère*). This is the case in insects and mammals. In the lizard the ramification is rather more extended than in mammals, whilst in the frog it is spread over a considerable length of the fibre. The ramification shows a fibrillar structure, which is especially evident at the enlargements. In mammals there appears to be only one end-plate to each fibre, while in reptiles there may be

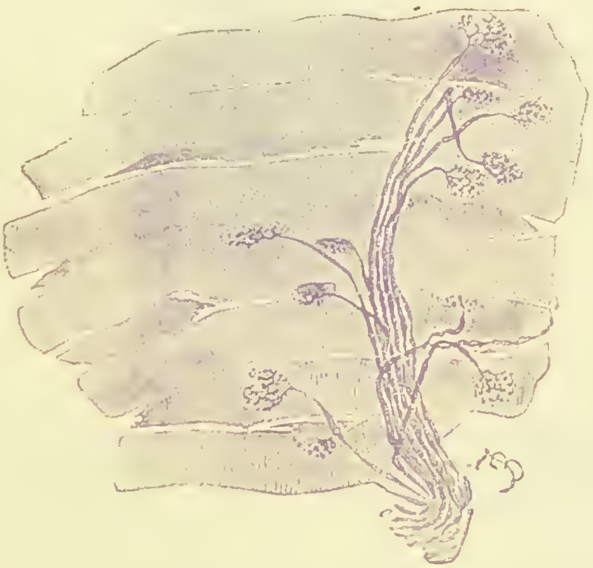

FIG. 265.—MOTOR NERVE-ENDINGS IN THE ABDOMINAL MUSCLES OF A RAT. GOLD PREPARATION. Magnified 170 diameters. (Szymonowicz.)

several. The end-plate is covered, externally to the sarcolemma, by an expansion of the sheath of Henle of the nerve-fibre (*telolemma*).

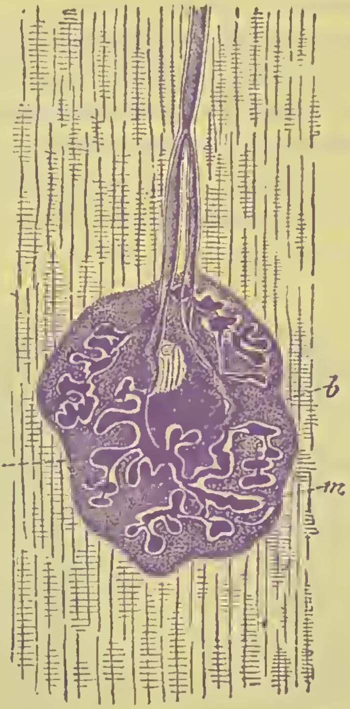

FIG. 266.—MOTOR END-ORGAN OF A LIZARD, GOLD PREPARATION. (Kühne.)

n, nerve-fibre dividing as it approaches the end-organ; *r*, ramification of axis-cylinder upon *b*, granular bed or sole of the end-organ; *m*, clear substance surrounding the ramifications of the axis-cylinder.

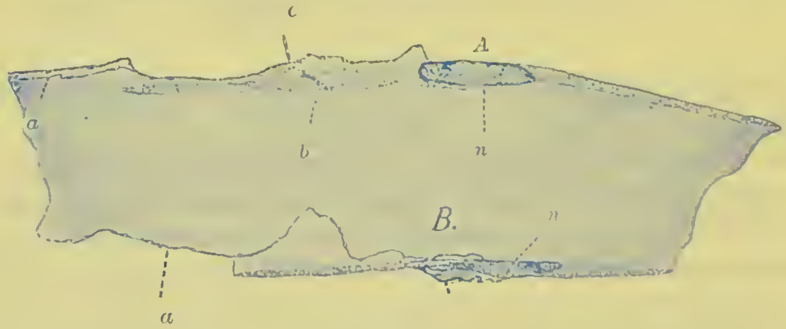

FIG. 267.—ENDING OF NERVE-FIBRILS OVER PLAIN MUSCLE-CELLS. (Huber and de Witt.)

a, fibrils passing to their termination; *b*, a terminal fibril; *c*, a branch passing to another muscle-cell; *n*, nuclei of cells.

In **involuntary muscle**, both plain and cardiac (fig. 268), the nerve-fibres, which near their termination are entirely non-medullated, end in plexuses. The primary plexuses are generally furnished with ganglion-cells in abundance. Such gangliated plexuses are best developed in connection with the intestine. From the cells of these plexuses other

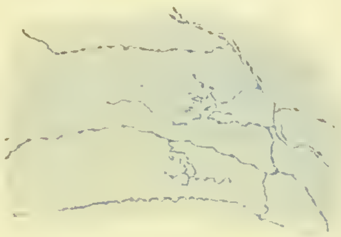

FIG. 268.—ENDING OF NERVE-FIBRES IN CARDIAC MUSCLE. (Smirnow.)

nerve-fibres pass which form secondary plexuses and terminal ramifications amongst the contractile fibre-cells, to the surface of which the endings of the branches, often slightly enlarged, are applied (Huber and de Witt).

LESSON XX.

STRUCTURE OF THE LARGER BLOOD-VESSELS.

1. Sections of a medium-sized peripheral artery and vein, *e.g.*, popliteal or radial. In this preparation the limits of the vascular coats can be well seen and also the differences which they present in the arteries and veins respectively. The sections may be stained with hæmalum and eosin or with orcein, and mounted in dammar or xylol balsam.

2. Mount in xylol balsam or dammar a thin slice cut from the inner surface of a large artery which, after having been cut open longitudinally and washed with distilled water, has been rinsed with nitrate of silver solution and then with distilled water and exposed for a minute or two to sunlight. It should then be hardened in alcohol, or it may be exposed in this to the light. This preparation will show the outlines of the epithelium-cells which line the vessel. A similar preparation may be made from a large vein.

3. A piece of an artery which has been macerated for some days in 33 per cent. alcohol is to be teased so as to isolate some of the muscular cells of the middle coat and portions of the elastic layers (networks and fenestrated membranes) of the inner and middle coats. The tissue may be stained cautiously with diluted hæmalum, and glycerine afterwards added. The muscular cells are recognisable by their irregular outline and long rod-shaped nuclei. Sketch one or two and also a piece of the elastic network or of fenestrated membrane. The fenestrated membrane is best obtained from one of the arteries of the base of the brain; it is also well seen in the arteries within the kidney.

4. Transverse sections of aorta and carotid. Notice the differences in structure between these and the section of the smaller artery.

5. Transverse section of vena cava inferior. Notice the comparatively thin layer of circular muscle, and outside this the thick layer of longitudinal muscular bundles in the adventitia.

Make sketches from 1, 4, and 5 under a low power, from 2 and 3 under a high power.

An **artery** is usually described as being composed of three coats, an *inner* or elastic, a *middle* or muscular, and an *external* or areolar (figs. 269, 270, *b*, *c*, *d*). It is, however, more correct to describe the wall of an artery as being mainly composed of muscular and elastic tissue, lined internally by a pavement epithelium (*endothelium*), and strengthened externally by a layer of connective tissue (*adventitia*).

The *inner coat* (*tunica intima*) is lined by a thin layer of *pavement epithelium* (*endothelium*), the cells of which are somewhat elongated in the direction of the axis of the vessel (fig. 271), and form a smooth lining to the tube. After death they become easily detached.

The endothelium is the essential layer in all blood-vessels. It is always the first part to be developed, and in some it remains as the only layer of the vessel. This is the case with all true capillaries and with certain veins, and also with the lacunar spaces or *sinusoids*, which, as Minot has pointed out, take the place of capillaries in certain parts (*e.g.* in the liver, the medulla of the suprarenal capsules and the Wolffian body of the embryo); it is also true of the sinuses of erectile tissue, as well as the sinus-like blood-vessels which are met with in invertebrates. In some structures the endothelial layer of the blood-vessels is imperfect, viz.: in the capillaries and blood-sinuses of the spleen, the placental mucous membrane of the pregnant uterus, and probably the sinusoids (capillaries) of the liver; in these places

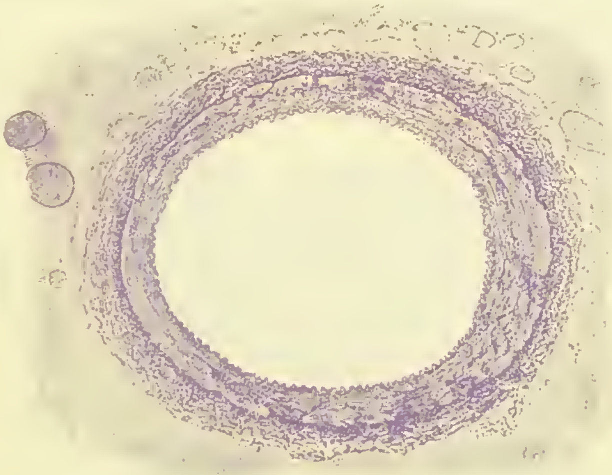

FIG. 269.—SECTION OF RENAL ARTERY OF DOG. (G. Mann.) Low power photograph.

The elastic layer of the thin inner coat is thrown into corrugations by the post-mortem contraction of the middle coat. The distinction between middle coat and adventitia is well shown. Some branches of the renal nerves are seen, cut across, in the tissue around the artery.

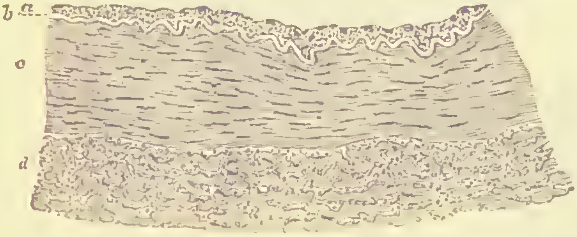

FIG. 270.—TRANSVERSE SECTION OF PART OF THE WALL OF THE POSTERIOR TIBIAL ARTERY. 75 diameters.

a, epithelial and subepithelial layers of inner coat; *b*, elastic layer (fenestrated membrane) of inner coat, appearing as a bright line in section; *c*, muscular layer (middle coat); *d*, outer coat, consisting of connective-tissue bundles. In the interstices of the bundles are some connective-tissue nuclei, and, especially near the muscular coat, a number of elastic fibres cut across.

the blood finds its way into the interstices of the organ and comes in direct contact with the tissue-cells.

Next to the endothelium comes an elastic layer in the form either of *elastic networks* (fig. 273) or of a *fenestrated membrane* (fig. 272). In some arteries there is a layer of fine connective tissue intervening between the epithelium and the fenestrated membrane (*subepithelial layer*).

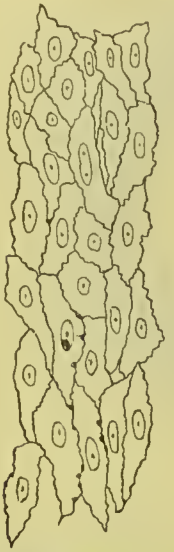

Fig. 271.—Epithelial layer lining the posterior tibial artery. 250 diameters.

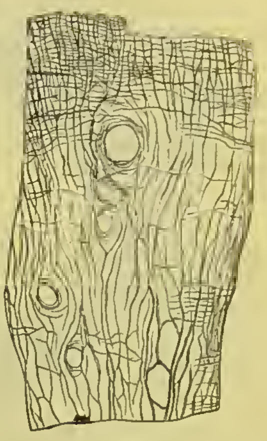

Fig. 272.—Portion of fenestrated membrane of Henle from an artery. (Toldt.)

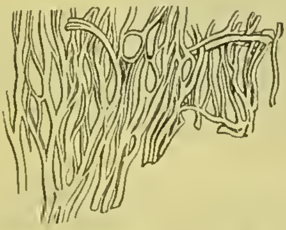

Fig. 273.—Elastic network of artery. (Toldt.)

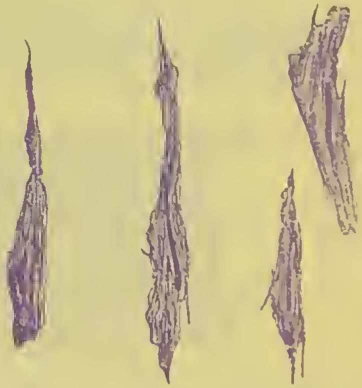

Fig. 274.—Muscular fibre-cells from superior thyroid artery. 340 diameters.

The *middle coat* (*tunica media*) consists mainly of circularly disposed plain muscular fibres, but it is also pervaded in most arteries by a network of elastic fibres which are connected with the fenestrated membrane of the inner coat and are sometimes almost as much developed as the muscular tissue itself. This is especially the case with the larger arteries, such as the aorta and the carotid and its immediate branches, but in the smaller arteries of the limbs the middle coat is composed almost purely of muscular tissue. The muscular fibres are comparatively short, with long rod-shaped nuclei, and are often irregular in shape (as in fig. 274), especially if the middle coat contains much elastic tissue.

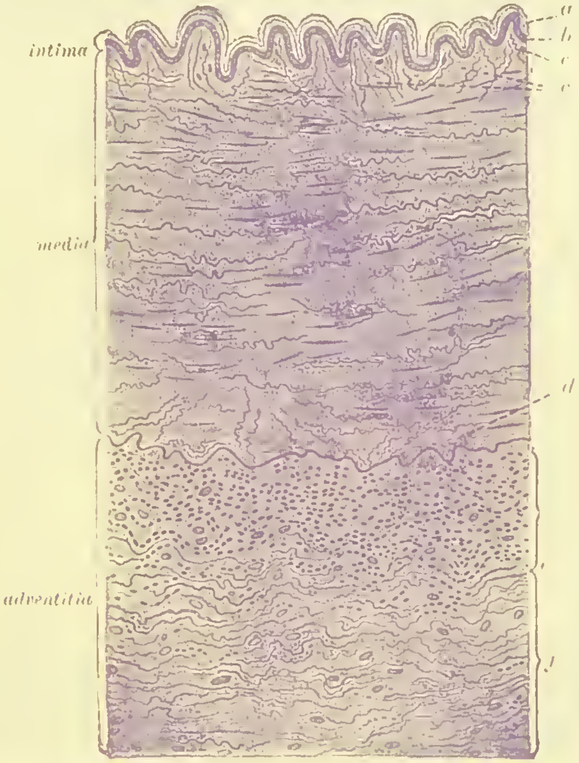

FIG. 275.—SECTION OF THE LINGUAL ARTERY. (Grünstein.)

a, epithelium and subepithelial layer of inner coat; *b*, its elastic layer; *c*, *c*, *d*, innermost and outermost layers of middle coat, with elastic fibres passing obliquely to join the elastic layers which bound that coat; *e*, innermost part of outer coat or adventitia, showing many elastic fibres cut across; *f*, outer part of adventitia.

The *outer coat* is formed of connective tissue with a good many elastic fibres, especially next to the middle coat. The strength of an artery depends largely upon this coat; it is far less easily cut or torn than the other coats, and it serves to resist undue expansion of the vessel. Its outer limit is not sharply marked, for it tends to blend with the surrounding connective tissue; hence it has been termed *tunica adventitia.*

Variations in structure.—The *aorta* (figs. 276, 277) differs in some respects in structure from an ordinary artery. Its inner coat contains a considerable thickness of subepithelial connective tissue, but the elastic layers of this coat are chiefly composed of fine fibres, and are not especially marked off from those of the middle coat, so that the inner and middle coats appear blended with one another. On the other hand, there is a very great development of elastic tissue in the middle coat, forming membranous layers which alternate with layers of the muscular tissue. A good deal of connective tissue also takes part in the formation of the middle coat, making this coat unusually strong. The inner and middle coats constitute almost the entire thickness of the wall, the outer coat being relatively thin.

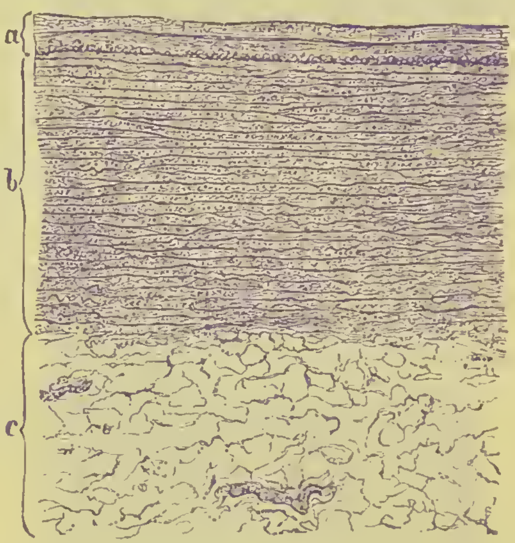

Fig. 276.—Section of thoracic aorta as seen under a low power. (Toldt.)

a, the inner coat consisting of three layers, viz.: 1. Epithelium seen as a fine line. 2. Subepithelial layer. 3. Elastic layers. In the outer part of the inner coat, at its junction with the middle, a layer of longitudinal muscular fibres is represented as cut across. *b*, middle coat with alternating layers of muscle and elastic membranes; *c*, outer coat with two vasa vasorum.

The other variations which occur in the arterial system have reference chiefly to the development and arrangement of the muscular tissue. Thus in many of the larger arteries there are a few longitudinal muscular fibres at the inner boundary of the middle coat, and in some arteries amongst the circular fibres of the middle coat. This is the case in the aorta. In the part of the umbilical arteries within the umbilical cord there is a complete layer of longitudinal fibres internal to the circular fibres and another external to them, whilst the amount of elastic tissue is very small. Longitudinal fibres are also present in some other arteries (iliac, superior mesenteric, splenic, renal, etc.), external to the circular fibres, and therefore in the outer coat of the artery.

The **veins** (fig. 278) on the whole resemble the arteries in structure, but they present certain differences. In the *internal coat* the same layers may be present, but the elastic tissue is less developed, and

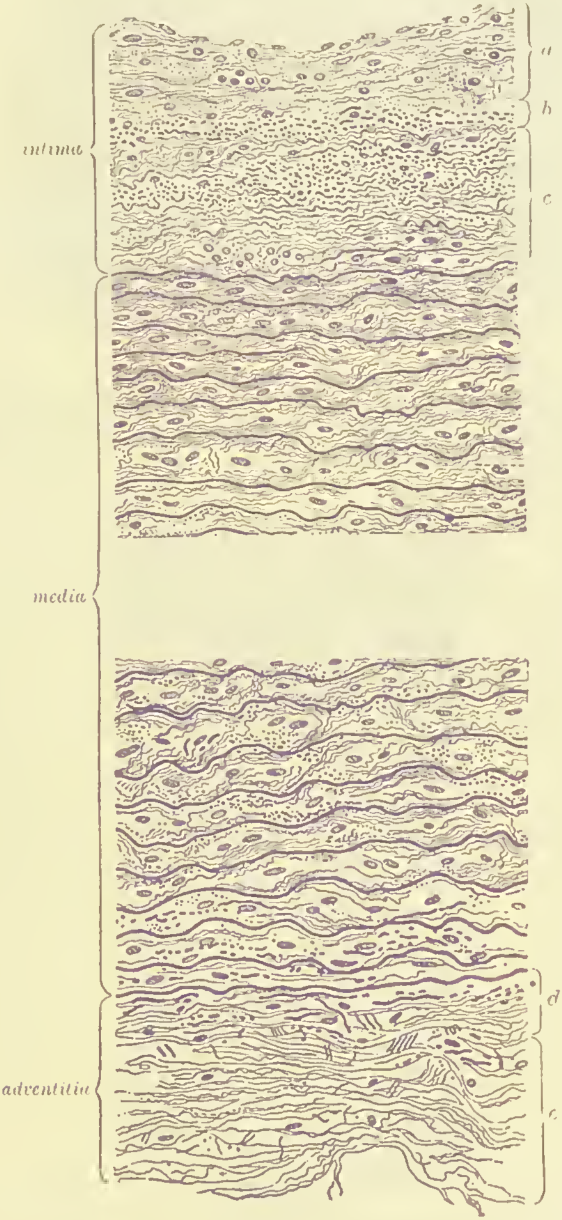

FIG. 277.—SECTION OF AORTA MORE MAGNIFIED. (Grünstein.)

a, epithelial and subepithelial layers of inner coat; *b*, *c*, outer layers of inner coat containing many fine elastic fibres; *d*, *e*, parts of outer coat.

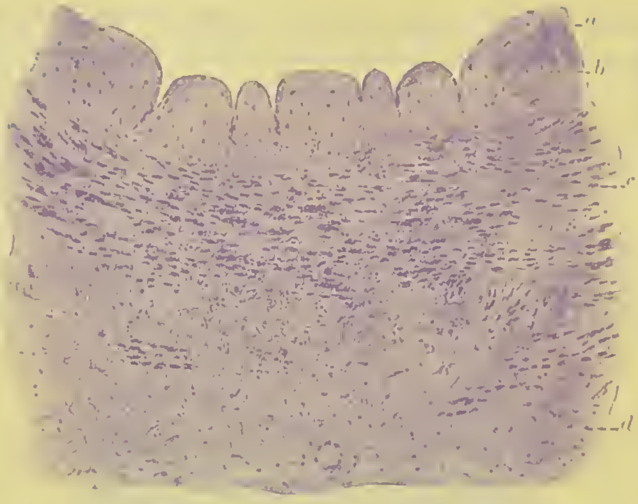

FIG. 278.—TRANSVERSE SECTION OF PART OF THE WALL OF ONE OF THE POSTERIOR TIBIAL VEINS (MAN). About 200 diameters.

a, epithelial, and *b*, subepithelial layers of inner coat; *c*, middle coat consisting of irregular layers of muscular tissue, alternating with connective tissue, and passing somewhat gradually into the outer connective tissue and elastic coat, *d*.

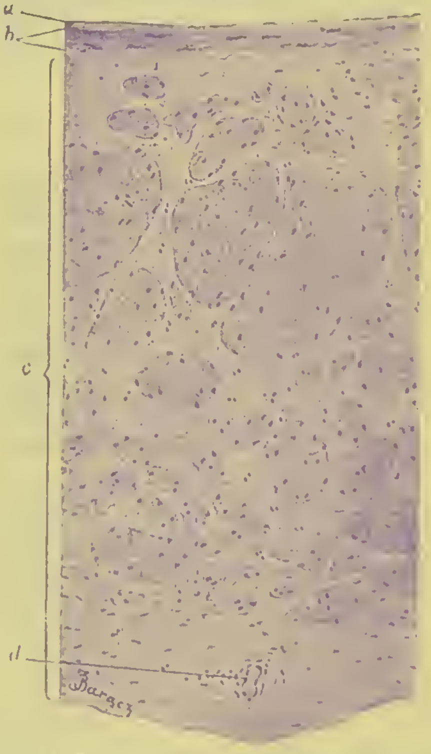

FIG. 279.—TRANSVERSE SECTION OF THE INFERIOR VENA CAVA OF THE DOG. (Szymonowicz.) Magnified 150 diameters.

a, intima; *b*, thin layer of circular muscle; *c*, thick adventitia with longitudinal muscular bundles; *d*, a vas vasis.

may be quite inconspicuous; it seldom takes the form of a complete membrane. The epithelium cells are less elongated than those of the arteries. The *middle coat* (*c*) contains less elastic tissue and also much less muscular tissue, being partly occupied by bundles of white connective-tissue fibres. These are continuous with those of the external coat, which is relatively better developed in the veins than in the arteries, so that, although thinner, their walls are often stronger.

Many of the veins are provided with *valves*, which are crescentic folds of the internal coat strengthened by a little fibrous tissue: a few muscular fibres may be found in the valve near its attachment. The layer of the inner coat is rather thicker and the epithelium-cells are more elongated on the side which is subject to friction from the current of blood than on that which is turned towards the wall of the vessel.

Variations in different veins.—The veins vary in structure more than do the arteries. In many veins longitudinal muscular fibres are found in the inner part of the middle coat, as in the iliac, femoral, umbilical; the umbilical vein within the umbilical cord having three muscular layers like the corresponding arteries; it has a well-developed internal elastic layer. In other veins, longitudinal fibres occur external to the circularly disposed fibres, and may be described as belonging to the outer coat. This is the case with the abdominal and especially the hepatic portions of the inferior vena cava (fig. 279), and to a less extent with the hepatic veins and the portal vein and its tributaries. In the superior vena cava, in the upper part of the inferior vena cava and in the jugular, subclavian, and innominate veins muscular fibres are almost entirely absent in the middle coat, and there are but few in the adventitia. The veins of the pia mater, brain and spinal cord, retina, and bones, and the venous sinuses of the dura mater and placenta have no muscular tissue.

It is only the larger veins, especially those of the limbs, that possess valves. They are wanting in most of the veins of the viscera (although occurring abundantly in some of the tributaries of the portal vein) in those within the cranium and vertebral canal, in the veins of the bones, and in the umbilical vein.

LESSON XXI.

SMALLER BLOOD-VESSELS AND LYMPH-VESSELS. SEROUS MEMBRANES. MICROSCOPIC STUDY OF THE CIRCULATION. DEVELOPMENT OF BLOOD-VESSELS.

1. Take a piece of pia mater which has been fixed with 2 per cent. bichromate of potassium and stained with hæmatoxylin, and separate from it some of the small blood-vessels of which it is chiefly composed. Mount the shreds in dilute glycerine, or after dehydrating with alcohol and passing through clove-oil they can be mounted in dammar or xylol balsam. The structure of the small arteries can be studied in this preparation, the nuclei of the epithelium and of the muscular coat being brought distinctly into view by the stain. The veins of the pia mater possess no muscular tissue. Capillary vessels which have been dragged out from the brain in removing the pia mater may also be seen in this preparation. Sketch two small arteries of different sizes, giving also their measurements.

2. Mount in dammar or xylol balsam a piece of the omentum of the rabbit, stained with silver nitrate. The membrane should be stretched over a cork or a ring of wood or vulcanite. Or it may conveniently be fixed by spreading it over a glass plate, and having brought its margins round the edges of the plate, place another plate of the same size at the back, and bind the plates together by a couple of rubber bands; the exposed surface can then be treated in the following way: Rinse with distilled water, cover for five minutes with 1 per cent. nitrate of silver solution, again wash with water and expose to sunlight. When slightly stained, the preparation is removed from the light, placed in spirit, and afterwards transferred to clove-oil. Pieces may now be cut off from the membrane, spread flat on a slide, and mounted in balsam or dammar; they should include one or more blood-vessels.

This preparation is intended to show the epithelium of the smaller blood-vessels and accompanying lymphatics, and also the epithelium of the serous membrane. Sketch a small piece showing the epithelium of the vessels.

3. Mount in balsam or dammar a piece of the central tendon of the rabbit's diaphragm which has been prepared with silver nitrate, the pleural surface having been first brushed to remove the superficial epithelium and thus enable the nitrate of silver more readily to penetrate to the network of underlying lymphatic vessels. Observe the lymphatic plexus under a low power; sketch a portion of the network. If the peritoneal surface is focussed, the epithelium which covers that surface will be seen, and opposite the clefts between the radially disposed tendon-bundles stomata may be looked for in this epithelium.

4. Examine sections of the thoracic duct. These may be made in the same way as sections of the blood-vessels.

5. Stomata.—Open the abdomen of a freshly killed frog, preferably a male, and remove the abdominal viscera, taking care not to injure the membrane or septum at the back of the abdomen, which lies over and between the kidneys and separates the peritoneal cavity from the *cisterna lymphatica magna*, a large lymph-space in which the aorta and vena cava are

contained. Cut out the kidneys along with as much as possible of the above septum; rinse with distilled water; and place in a watch-glass of 1 per cent. silver nitrate for 5 minutes. Rinse again in distilled water and expose in tap water to the light. When slightly browned snip off a portion of the membranous septum, float it flat on a slide, drain off the superfluous water and allow it to dry; then add a drop of xylol balsam or dammar and cover the preparation.

6. Kill a frog by destroying the brain and study the circulation of the blood in the mesentery. It can also be studied in the web of the frog's foot, and in the lung and tongue of the frog or toad or in the tail of the tadpole or of any small fish. But for observing the phenomena attending commencing inflammation and the emigration of leucocytes from the vessels, the mesentery is the most convenient object. The frog can be immobilised with curari or by placing it in water in which chloroform or ether has been shaken up: a lateral incision is made in the abdominal wall, a loop of intestine drawn out, and laid over a ring of cork which is fixed to a glass plate and covered with a thin piece of glass (fig. 280). The membrane must be kept wet with salt solution.[1]

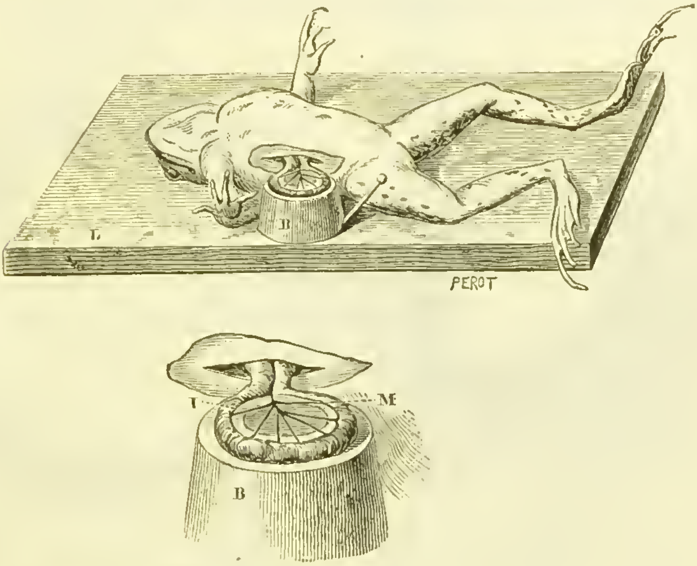

FIG. 280.—METHOD OF STUDYING THE CIRCULATION IN THE FROG'S MESENTERY. (Ranvier.)

L, cork or glass plate; *B*, perforated cork, the aperture in which is closed by a circular glass cover (not too thin); *M*, mesentery laid over glass. The brain is destroyed and the animal then immobilised with curari.

7. The arrangement of the blood-vessels in the various tissues and organs are studied in injected preparations (see Appendix).

The coats of the **small arteries and veins** are much simpler in structure than those of the larger vessels, but they contain at first all the same elements. Thus there is a lining endothelium and an elastic layer, the two together forming an *inner coat*; a *middle coat* of circularly disposed plain muscular tissue; and a thin *adventitia*. The same differences are found between the smaller arteries and veins as with the larger, the walls of the veins being thinner and containing far less muscular tissue (fig. 281), and the lining epithelium-cells, much elongated in both vessels, are far longer and narrower in the small arteries than in the corresponding veins (fig. 282).

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[1] For details of the methods of studying the circulation see *A Course of Practical Histology*.

In the smallest vessels it will be found that the elastic layer has entirely disappeared in the veins, and the muscular tissue is considerably reduced in thickness in both kinds of vessel. Indeed, it is soon represented by but a single layer of contractile cells, and even these no longer form a complete layer. By this time also, the outer coat as well as the elastic layer of the inner coat have disappeared both from arteries and veins. The vessels are reduced, therefore, to the condition of a tube formed of pavement-epithelium cells, with a partial covering of circularly disposed muscular cells.

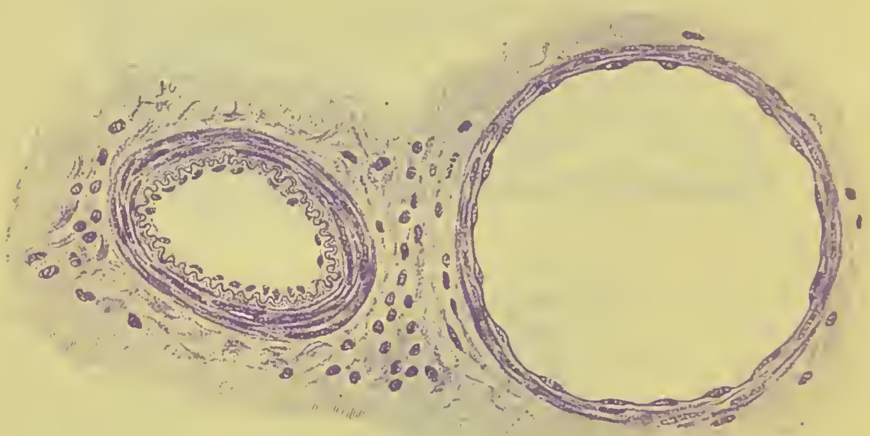

FIG. 281.—TRANSVERSE SECTION OF A SMALL ARTERY AND VEIN. Magnified 250 diameters.

Even in the smallest vessels, which are not capillaries, the differences between arteries and veins are still manifested. These differences may be enumerated as follows: The veins are larger than the corresponding arteries; they branch at less acute angles; their muscular cells are fewer, and their epithelium cells less elongated; the elastic layer of the inner coat is always less marked, and sooner disappears as the vessels become smaller.

Capillary vessels.—When traced to their smallest branches the arteries and veins eventually are seen to be continued into a network of the smallest blood-vessels or capillaries. The walls of these are composed only of flattened epithelium-cells (fig. 284) continuous with those that line the arteries and veins; these cells can be exhibited by staining a tissue with nitrate of silver. The cell-outlines are not shown in developing capillaries; in these, silver nitrate stains the whole wall. This is the case also with the capillaries of the villi, those of

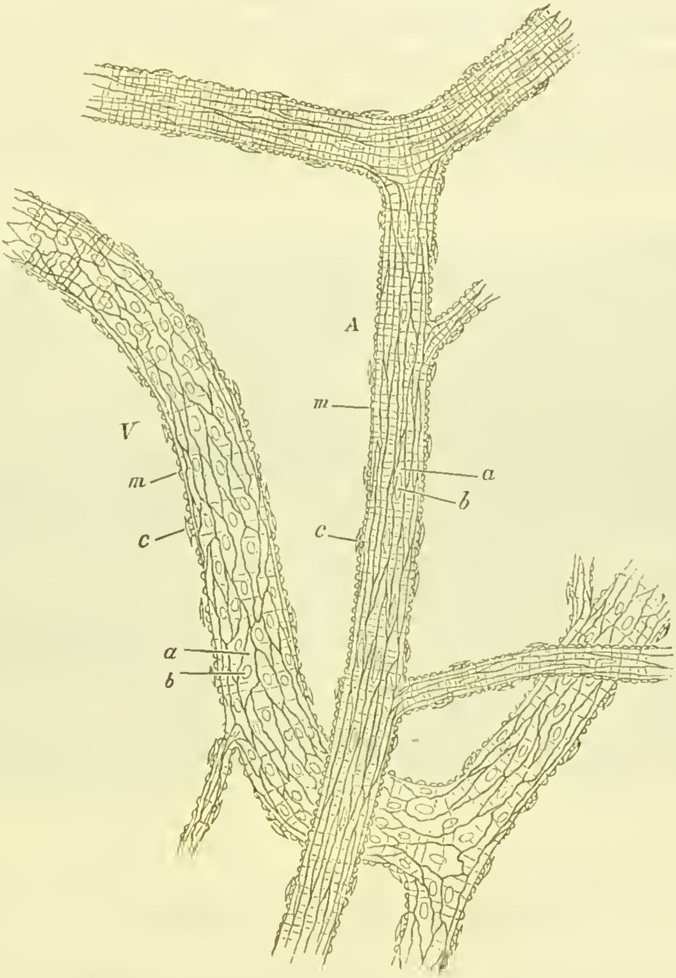

Fig. 282.—A small artery, *A*, and vein, *V*, from the subcutaneous connective tissue of the rat, treated with nitrate of silver, with subsequent staining of nuclei. 175 diameters.

a, *a*, epithelial cells with *b*, *b*, their nuclei; *m*, *m*, transverse markings due to staining of substance between the muscular fibre-cells; *c*, *c*, nuclei of connective-tissue corpuscles attached to exterior of vessel.

the choroid coat of the eye (Eberth), and those of the kidney-glomeruli (Ranvier): in all these places the walls are formed of a syncytium.

The capillaries vary somewhat in size and in the closeness of their meshes; their arrangement in different parts, which is mainly determined by the disposition of the tissue-elements, may best be studied in injected preparations, and will be described when the structure of the several organs is considered.

Usually the arterioles pass gradually into the capillary network and the capillaries unite to form small veins which, on receiving others, gradually increase in size. But in certain situations the arrangement is different. Thus in the spleen the arterial capillaries have imperfect walls and the blood passes into the interstices of the reticular tissue of the organ, from which it is collected by sinus-like veins which also have incomplete walls. In erectile tissue the arterioles open, without the medium of capillaries, into large cavernous spaces bounded by fibrous and plain muscular tissues and lined by epithelium: the veins lead out of these spaces, so that there are no true capillaries, except such as are distributed to the tissues which form the walls of the spaces. In the sympathetic ganglia, as shown by Ranvier (fig. 283), the capillaries open abruptly into large sinus-like venules. And in the liver and a few other organs, as will presently be explained, the connection between afferent and efferent vessels is effected, not by true capillaries, but by sinus-like spaces between the tissue elements ("sinusoids" of Minot).

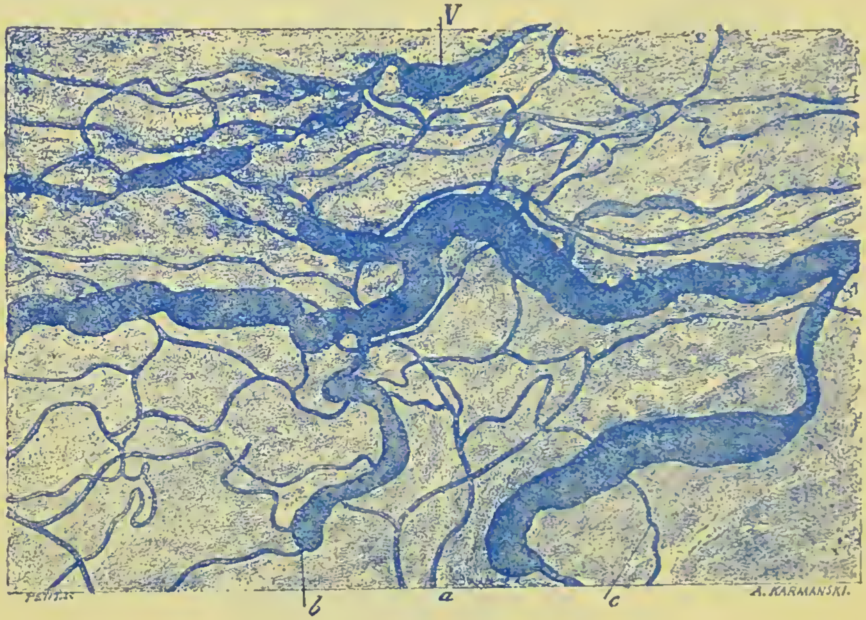

FIG. 283. —THIRD THORACIC SYMPATHETIC GANGLION OF RABBIT INJECTED. (Ranvier.)

a, arterioles; *b*, *c*, capillaries; *V*, sinus-like veins.

In the transparent parts of animals, the blood may be seen flowing through the capillary network from the arteries into the veins. The current is very rapid in the small arteries, somewhat less rapid in the veins, and slow in the capillaries. The current is fastest in the centre of the vessels, slowest near the wall (inert layer). In this layer the leucocytes are carried along by the stream and may be observed—especially where there is commencing inflammation of the part, as in the mesentery in consequence of exposure—to adhere to the inner surface of the blood-vessels, and here and there to pass through the coats of the small vessels, and appear as *migratory cells* in the surrounding connective tissue (fig. 285). The blood-platelets are also to be seen in the inert layer, and show a tendency to adhere to the wall and to one another in commencing inflammation.

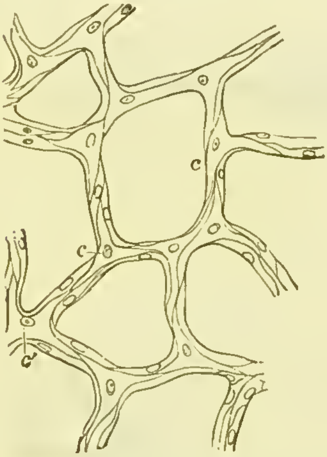

FIG. 284.—CAPILLARY VESSELS FROM THE BLADDER OF THE CAT, MAGNIFIED.

The outlines of the cells are stained by nitrate of silver.

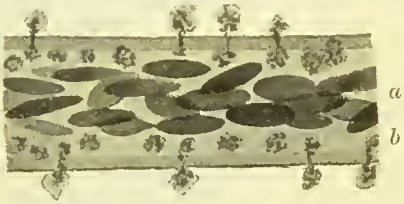

FIG. 285.—BLOOD FLOWING THROUGH A SMALL VEIN OF THE FROG'S MESENTERY.

The mesentery had been exposed for a short time, so that there was commencing inflammation and many of the white corpuscles are observed sticking to and even passing through the vascular wall. *a*, central rapid layer containing the coloured corpuscles; *b*, outer slower layer (inert layer) containing the white corpuscles.

Vessels and nerves of the blood-vessels.—The larger arteries and veins possess blood-vessels (*vasa vasorum*) and lymphatics, both of which ramify chiefly in the external coat. Nerves are distributed to the muscular tissue of the middle coat, after forming a plexus in the outer coat. Most of the nerves are non-medullated. But there are a certain number of medullated fibres intermingled with the non-medullated and passing to end in localised arborescences (fig. 286) partly in the adventitia, partly in the intima. These medullated fibres are doubtless afferent ; the majority of the non-medullated are probably efferent (vaso-motors). In the aorta of man and in some of the larger trunks Pacinian corpuscles are here and there met with in the adventitia. The capillary vessels also receive nerve-fibres, which form a fine plexus of fibrils in close contact with the endothelium-cells of which the walls of these vessels are composed. Small cells are found at intervals in connection with these plexuses (fig. 287), but whether they are of the nature of nerve-cells or not is uncertain.

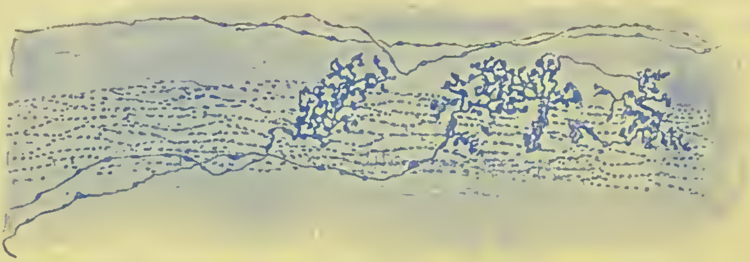

FIG. 286.—ENDING OF SENSORY NERVE-FIBRES IN ARBORESCENCES IN THE WALL OF A SMALL ARTERY. (Dogiel.)

The endothelium-cells of the vessel are outlined by dotted lines and the outlines of the muscular fibres are faintly indicated.

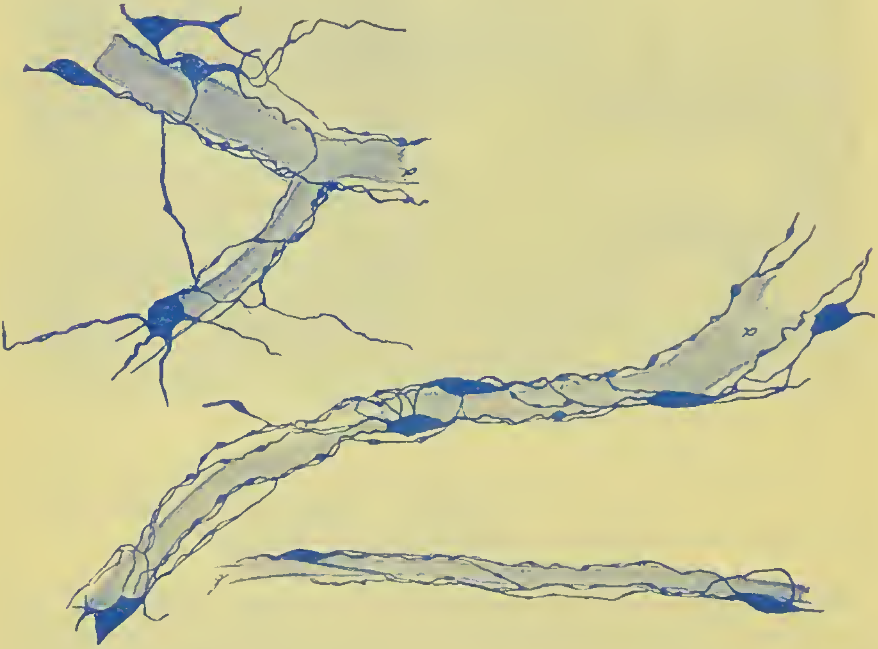

FIG. 287.—ENDING OF NERVE-FIBRILS ON CAPILLARY VESSELS. (Dogiel.)

Development of the blood-vessels.—The blood-vessels are developed in the connective tissue or in the mesenchyme which precedes it, the first vessels being formed in the vascular area which surrounds the early embryo. Their development may be studied in the embryo chick or mammal, in the omentum of the new-born rabbit, or in the serous membranes and subcutaneous connective tissue of fœtal animals. The cells which are to form the vessels (*vasoformative cells*) branch and unite with one another to form a syncytium, and cavities form in this and extend into the branches. In the meantime the nuclei multiply and become distributed along the branches, cell-areas being at a latter stage marked out around the nuclei. In this way intercommunicating vessels—capillaries in which blood-corpuscles have become also developed (see page 42)—are produced (fig. 288). These presently become connected with previously formed vessels, which extend themselves by sending out sprouts, at first solid, and afterwards hollowed out. Even the larger blood-vessels appear first to be developed in the same way as the capillaries, in so far that the epithelium is first formed and the muscular and other tissues are subsequently added; but whether they are formed as clefts in the mesoblastic tissue, which become bounded by flattened cells, or whether as a hollowed-out syncytium has not been definitely ascertained.

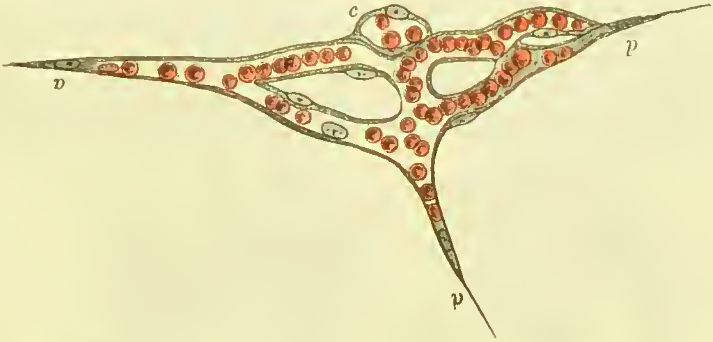

FIG. 288.—ISOLATED CAPILLARY NETWORK FORMED BY THE JUNCTION OF A HOLLOWED-OUT SYNCYTIUM, CONTAINING COLOURED BLOOD-CORPUSCLES IN A CLEAR FLUID.

c, a hollow cell the cavity of which does not yet communicate with the network; *p*, *p*, pointed cell processes, extending in different directions for union with neighbouring capillaries.

Many authors consider that new blood-vessels are exclusively formed by sprouts from pre-existing vessels, and regard the appearances above described as being due to retrogressive development of an already formed vascular network (see p. 43).

Sinusoids.—These are sinus-like blood-spaces between the cells of a tissue, which may when fully developed bear a superficial resemblance to blood-capillaries, but which differ essentially from them both in their mode of development and in their relationship to the connective tissue, as well as to the tissue-elements of the organs in which they occur.

Whereas capillary blood-vessels are developed amongst and between the tissue-elements and are connected with and grow from neighbouring capillaries which are themselves surrounded by areolar tissue, sinusoids make their first appearance in the form of comparatively large blood-spaces connected with the venous (or arterial) system. Into these, the walls of which are formed only of a single layer of endothelial cells, the tissue-elements of the developing organ (Wolffian body,

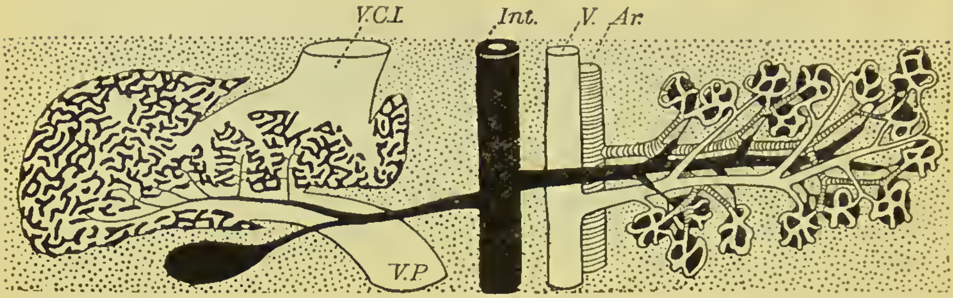

Fig. 289.—Diagram to illustrate the development of blood-capillaries (right side), and sinusoids (left side) respectively. (F. T. Lewis.)

Int, intestinal entoderm with outgrowth on the left to form the liver and gall-bladder, and on the right to form the pancreas. *V.C.I.*, vena cava inferior; *V.P.*, vena portæ; *V.*, vein and *Ar*, artery supplying pancreas. It is seen that the sinusoids or apparent capillaries of the liver are formed by the breaking up of a large blood-space into channels by the growth into it of cell-columns derived from the hepatic outgrowth of the entoderm.

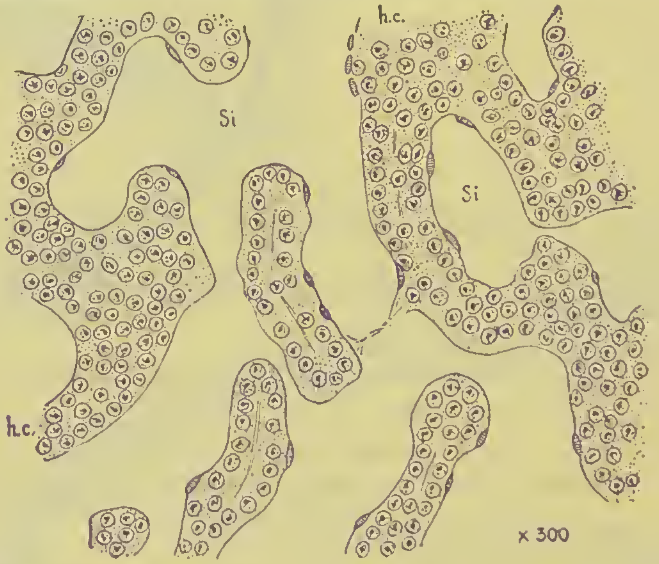

Fig. 290.—Section of the developing liver, to show how the hepatic cylinders encroach on the lumina of the sinus-like veins to break them up ultimately into capillary-like channels called sinusoids. (Minot.)

h.c., hepatic cylinders; *si*, sinusoids.

liver, suprarenals, blood-glands, etc.) grow, invaginating the thin wall and forming cell-trabeculæ within the sinus (figs. 289, 290), so that the cells of the organ are directly in contact with the invaginated endothelium, and are only separated by this from the blood contained within the sinus. But the connection may become yet closer than this, for, as happens in the liver, the invaginated endothelium may become defective, so that the blood within the sinus comes into actual contact with the cells of the organ, and runs into the interstices between them. As development proceeds these interstices may come to resemble blood-capillaries in general arrangement and shape; but the resemblance is only superficial, and the intimate relationship between the blood and the tissue elements, which are both enclosed within the original sinus, is usually maintained. The distinctive character of sinusoids was first recognised by Minot.

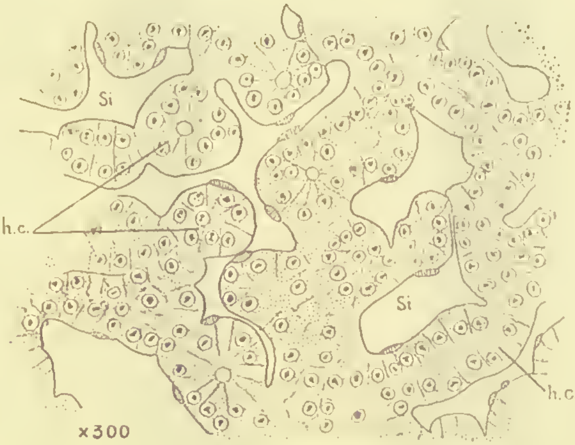

FIG. 291. - LIVER OF EMBRYO-CHICK OF ELEVEN DAYS. (C. S. Minot.)
h.c., hepatic cylinders; *Si*, sinusoids.

LYMPHATICS OR LYMPH-VESSELS.

To the lymphatic system belong not only the *lymph-vessels* and *lymph-glands*, but also the *cavities of the serous membranes*, which are moistened with lymph and are in open communication with lymph-vessels which run into their parietes.

The larger **lymph-vessels** somewhat resemble the veins in structure (fig. 291), except that their coats are much thinner and valves much more numerous. In lymphatics of smaller size, which in the fresh condition have a clear, perfectly transparent appearance and a very thin wall (fig. 292), the vessel is formed, first, by a lining of pavement-epithelium cells (lymphatic endothelium), which are elongated in the direction of the axis of the vessel; and, secondly, by a layer of circularly and obliquely disposed muscular fibres (fig. 293). In the smallest vessels (so-called *lymph-capillaries*, which are generally considerably larger than the blood-capillaries), there is nothing but the epithelium remaining, and the cells of this are frequently not more elongated in one direction than in another, but have a characteristic wavy outline (fig. 294).

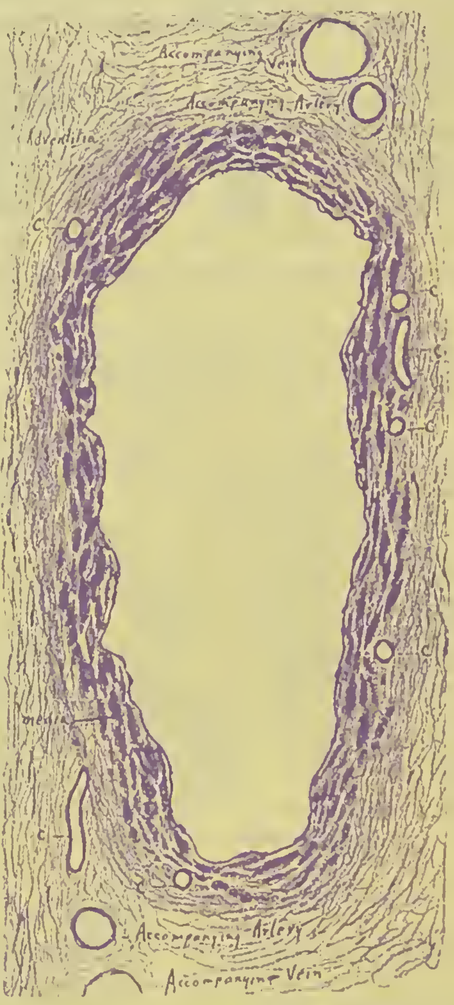

FIG. 292.—SECTION OF MODERATE-SIZED LYMPHATIC. (Evans.)
c, capillary vessels distributed to the muscular coat (media).

The lymphatics receive numerous nerve-fibres, which are non-medullated, and which end in a ramification of the finest fibrils, which are distributed to the coats of the vessels (fig. 295).

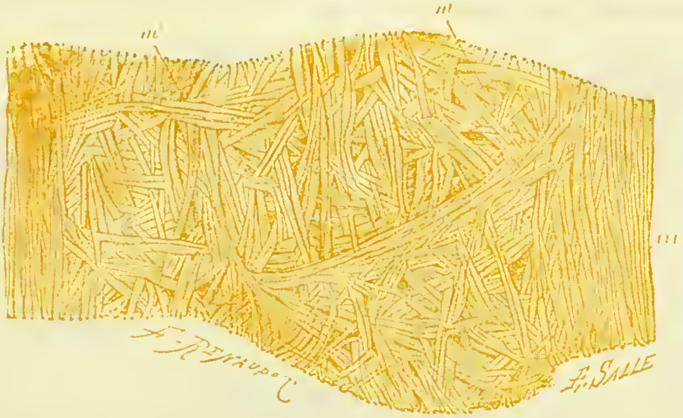

FIG. 293.—SUPRAVALVULAR DILATATION OF A LYMPHATIC OF THE MESENTERY OF A CAT; SILVER NITRATE PREPARATION. (Ranvier.)

m, circular muscle-fibres; *m'*, *m'*, irregular arrangement of muscle at the dilatation.

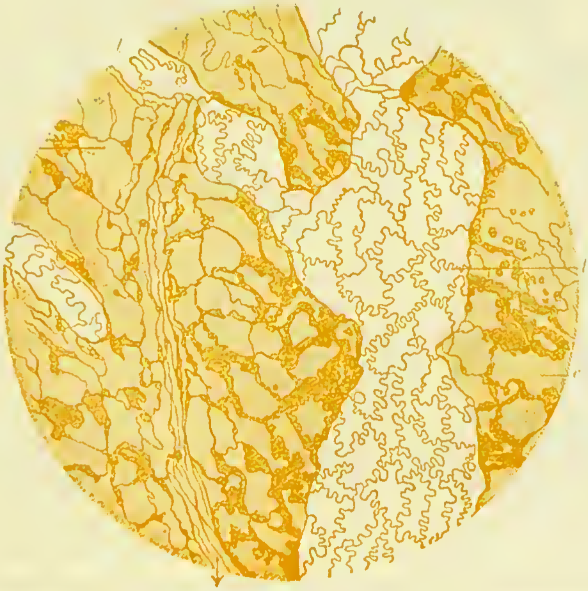

FIG. 294.—A SMALL PART OF THE LYMPHATIC PLEXUS OF THE PLEURAL LAYER OF THE DIAPHRAGM. Magnified 110 diameters. (Ranvier.)

l, lymphatics with characteristic epithelium; *c*, cell-spaces of the connective tissue here and there abutting against the lymphatic.

Lymphatics begin either in the form of *plexuses*, as in serous membranes (fig. 296), or of *lacunar interstices*, as in some of the viscera and all transitions occur between the two.

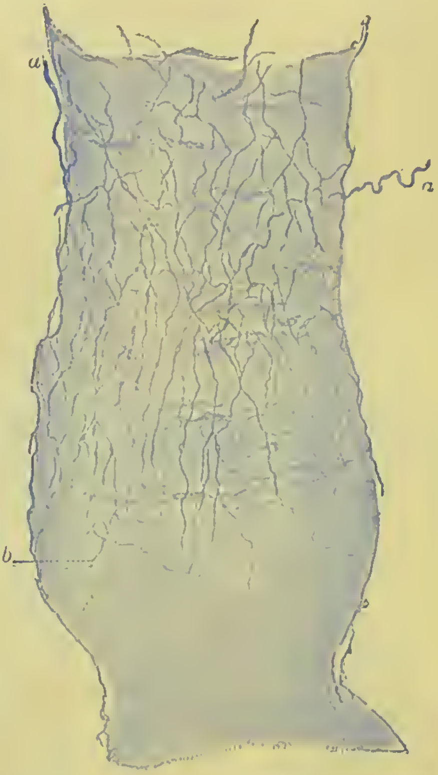

FIG. 295.—NERVES OF A LYMPHATIC VESSEL, SHOWN BY METHYLENE BLUE. (Dogiel.)

a, *a*, non-medullated fibres passing to the vessel; *b*, part of their terminal ramification.

In order to show their structure, it is usual to stain a tissue with nitrate of silver; for exhibiting their distribution they may be injected by sticking the nozzle of a very fine injecting cannula into any tissue which contains them, and forcing coloured fluid under gentle pressure into the interstices of the tissue.

In silver preparations it may be observed that the lymphatics always appear in the form of clear channels in the stained ground-substance of the connective tissue, and that their walls are in close connection with the cells and cell-spaces of that tissue (fig. 294). But except in the case of the serous membranes, no open communication is observable between the lymphatic vessels and the interstices of the connective tissue, although from the readiness with which they can be injected from the latter there must be a ready means of passage of the interstitial lymph into the commencing lymphatics.

Development.—The lymphatic vessels were originally described by Klein, and more recently by Retterer, as being developed from hollowed-out cells in the same manner as the blood-vessels, and by Gulland as becoming formed at the periphery as clefts in the connective tissue, which later form a connection with the venous system. But the

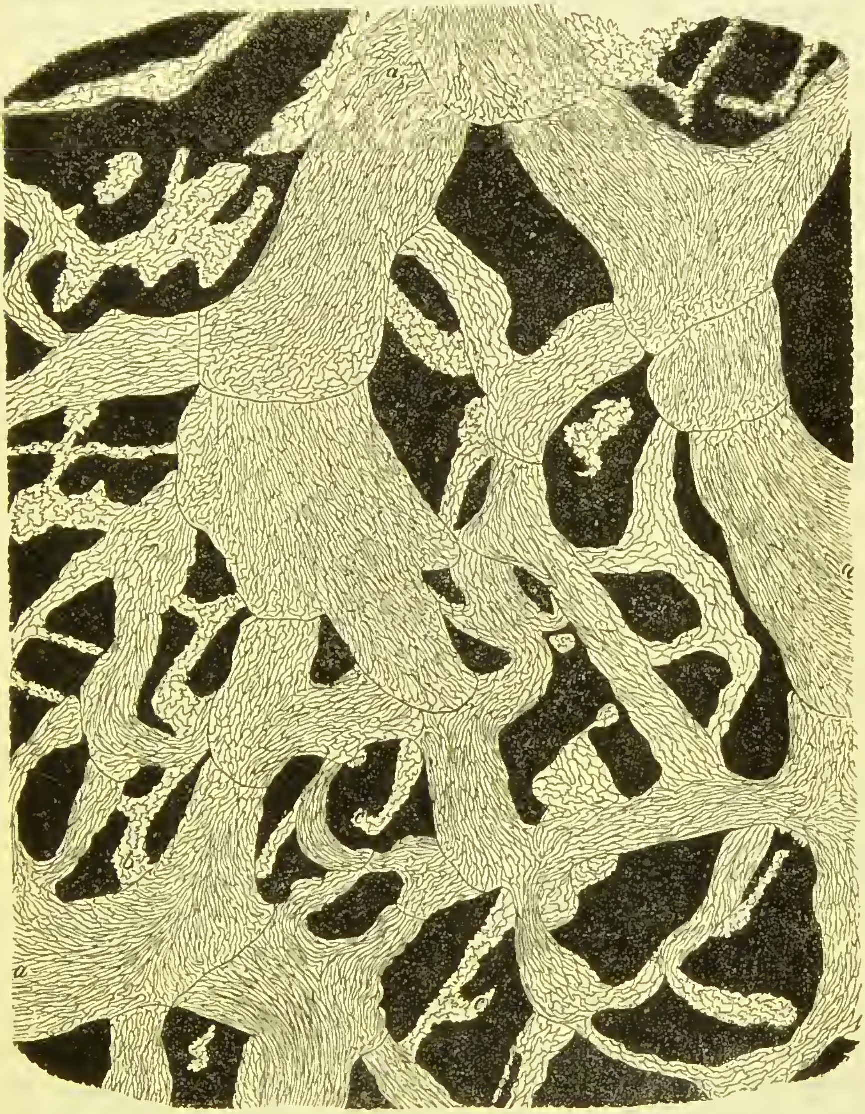

FIG. 296.—LYMPHATIC PLEXUS OF CENTRAL TENDON OF DIAPHRAGM OF RABBIT, PLEURAL SIDE. (Klein.)

a, larger vessels with lanceolate cells and numerous valves; *b*, *c*, lymph-capillaries with wavy-bordered cells.

investigations of Ranvier, recently confirmed by Miss Sabin, Lewis, and others, have shown that the lymphatic trunks grow out from the venous system, and gradually penetrate into the peripheral parts of the embryo.

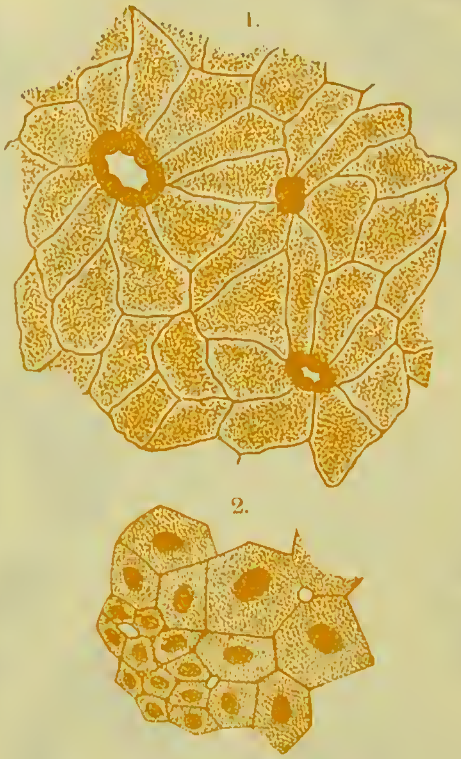

Fig. 297.

1. Epithelium from the posterior part of the frog's peritoneum. showing three stomata leading into the cisterna lymphatica magna. (v. Ebner, after Schweigger-Seidel and Dogiel.)
2. A portion of epithelium from the peritoneal surface of the rabbit's diaphragm. Three pores are visible between the epithelium cells. (v. Ebner, after Ludwig and Schweigger-Seidel.)

Serous Membranes.

The **serous membranes**, which may be conveniently studied in connection with the lymphatic system, are delicate membranes of connective tissue which surround and line the internal cavities of the body, and are reflected over many of the thoracic and abdominal viscera; in passing to which they form folds (such as the mesentery), within which blood-vessels, lymphatics, and nerves are conducted to the viscera.

The inner surface is lined by a continuous layer of *pavement-epithelium* (*endothelium*) (figs. 78, 79), which is very distinct in nitrate of silver preparations. In some places there are apertures in the epithelium which lead directly into subjacent lymphatic vessels. These apertures are called *stomata*, and are sometimes surrounded by special cells (fig. 297). They are numerous upon the peritoneal surface of the diaphragm, but are present in most serous membranes. They are nowhere better studied or more easily seen than in the peritoneal membrane at the back of the abdominal cavity in the frog. This membrane lies between and at the sides of the kidneys, and serves to separate the peritoneal cavity from the large lymph-space just behind it. If the membrane is prepared by the nitrate of silver method the stomata and the cells which surround them on either side of the membrane are well shown.

The pavement-epithelium of the serous membrane rests upon a homogeneous basement-membrane, which is especially well marked in the serous membranes of man. The rest of the thickness of the membrane is composed of connective tissue, with a network of fine elastic fibres near the inner surface (fig. 298).

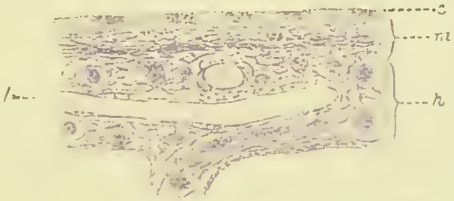

Fig. 298.—Section of pleura: ox (Favaro). Magnified 270 diameters.
e, endothelium; *m*, substance of membrane with numerous elastic fibres; *h*, hypo-pleura; *l*, lymph-vessel.

The cavities of the serous membranes are originally formed in the embryo as a cleft in the mesoderm (pleuro-peritoneal split, cœlom) which becomes lined with epithelium, outside which the cœlomic wall eventually becomes differentiated into the serous membranes.

LESSON XXII.

LYMPH-GLANDS, TONSILS, THYMUS.

1. SECTIONS of a lymph-gland which has been hardened either in formol or potassium bichromate, or in chromic acid or picric acid followed by alcohol, stained in bulk, and embedded in paraffin. Or the sections may be stained with hæmatoxylin and eosin. Notice (1) the fibrous and muscular capsule, with trabeculæ extending inwards from it through the cortex and anastomosing with one another in the medulla, (2) the dense lymphoid tissue (adenoid tissue of some authors) forming large masses in the cortex (cortical nodules) and rounded cords in the medulla (medullary cords). Notice also the clearer channel or lymph-sinus which everywhere intervenes between the fibrous tissue and the lymphoid tissue. Observe the fine fibres and branched cells which bridge across this channel.

Make a general sketch under a low power of a portion of the cortex together with the adjoining part of the medulla, and under a high power drawings of small portions of cortex and medulla.

The retiform tissue of the lymph-glands has already been studied (p. 91).

2. Sections of a hæmal lymph-gland. These may be readily found in the neck of the ox, in the neighbourhood of the large blood-vessels. Stain with eosin and hæmatoxylin or with eosin and methylene blue. Notice that the channels around the lymphoid nodules (or some of them) contain blood instead of lymph.

3. In sections of tonsil prepared similarly to those of the lymph-gland, notice the large amount of lymphoid tissue, partly collected into nodules. Observe also that the stratified epithelium, which covers the mucous membrane here as elsewhere in the mouth, is infiltrated with lymph-corpuscles. The tonsil is beset with pit-like recesses, with mucus-secreting glands opening into the pits.

4. Lymphoid nodules of mucous membranes. In other mucous membranes besides that of the back of the mouth and pharynx, collections of lymphoid tissue occur which resemble those of the tonsils; such nodules form the solitary glands of the stomach and intestines and the agminated glands of the small intestine, and are also found in the trachea and bronchial tubes and in the œsophagus. They may be studied later in sections of those parts.

5. Sections of the thymus gland of an infant or young animal. Notice that the masses of lymphoid (?) tissue which form the lobules of the gland are separated by septa of connective tissue, and that the lobules show a distinction into two parts, cortical and medullary. There are no lymph-paths within the lobules. Observe the differences of structure of the cortex and medulla, and especially notice the concentric corpuscles in the medullary part.

Make a sketch of one of the lobules under a low power and of a small part of the medulla under a high power, including one or two concentric corpuscles. Measure the latter.

Lymph-Glands.

Structure of a lymph-gland.—A lymph-gland (lymphatic gland) is composed of a framework of fibrous and plain muscular tissue, which incloses and supports the proper glandular substance, but is everywhere separated from it by a narrow channel, bridged across by cells and fibres, which is known as the *lymph-channel.* The *framework* consists of an envelope or *capsule* (fig. 299, *c*), and of *trabeculæ* (*tr*), which pass at intervals inwards from the capsule, and after traversing the cortex of the gland, divide and reunite with one another to form a network of fibrous bands. At one part of the gland there is usually a depression (*hilus*), and at the bottom of this the medulla comes to the surface and its fibrous bands are directly continuous with the capsule.

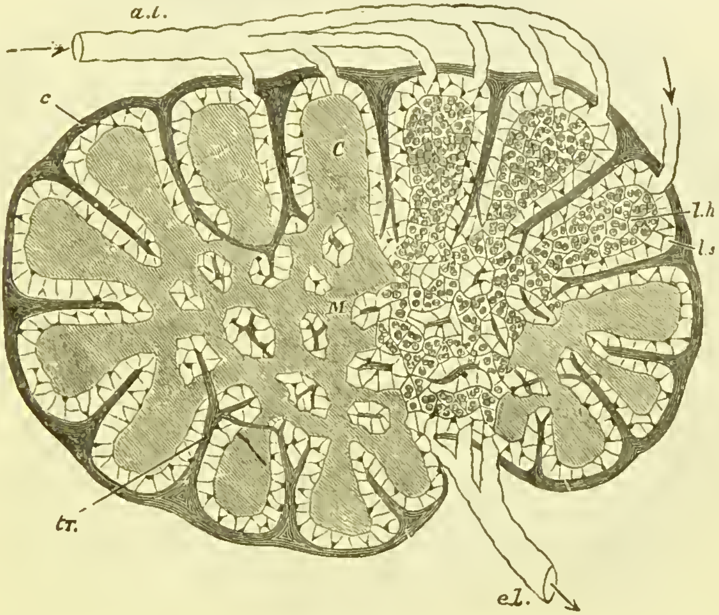

Fig. 299.—Diagrammatic section of lymph-gland. (Sharpey.)

a.l., afferent, *e.l.*, efferent lymphatics; *C*, cortical substance; *M*, reticulating cords of medullary substance; *l.h.*, lymphoid tissue; *l.s.*, lymph-sinus; *c*, capsule sending trabeculæ, *tr*, into the substance of the gland.

The proper *glandular substance* (*l.h.*) is composed of lymphoid tissue, *i.e.* a fine reticulum with the meshes thickly occupied by lymph-corpuscles. It occupies all the interstices of the gland, forming comparatively large rounded masses in the cortex (lymphoid nodules, *C*), which may be two or three deep, and smaller reticulating cord-like masses (lymphoid cords, *M*) in the medulla.

The cells which bridge across the lymph-channel in the medulla (fig. 300, *c*) are branching nucleated cells which often contain pigment, so that this part of the gland has a dark colour. Some may contain disintegrating erythrocytes. The lymph-channel is bridged across not only by these branched cells, but also by fibres derived from the capsule and trabeculæ, which pass to the lymphoid tissue and become lost in its reticulum. But the fibres are often completely concealed by the cells.

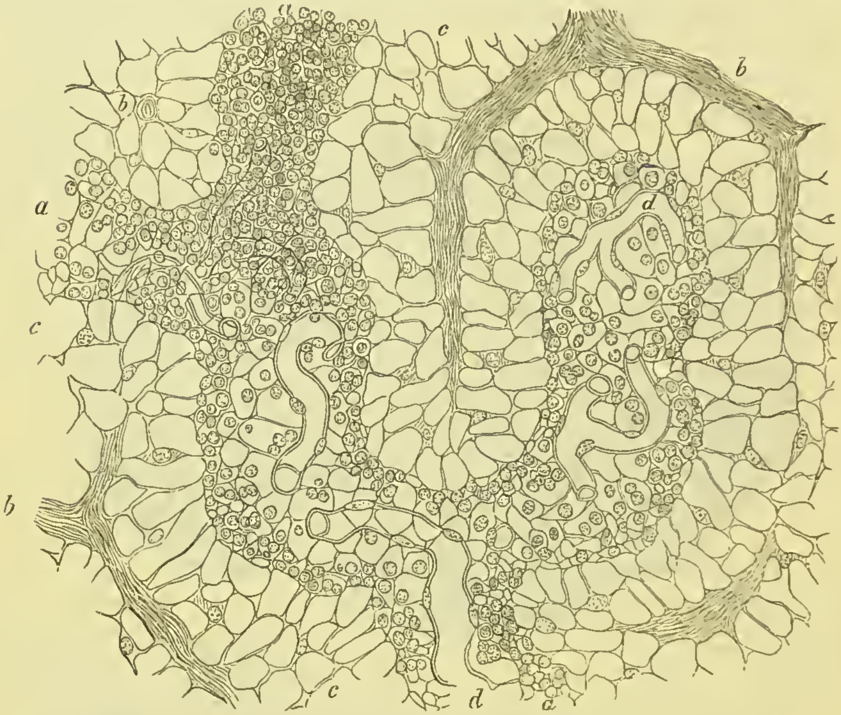

FIG. 300.—SECTION OF THE MEDULLARY SUBSTANCE OF A LYMPH-GLAND. 300 diameters. (Recklinghausen.)

a, *a*, *a*, lymphoid cords; *c*, lymph-sinus; *b*, *b*, trabeculæ; *d*, *d*, capillary blood-vessels.

Afferent lymph-vessels (fig. 299, *a.l.*) enter the lymph-channels after ramifying in the capsule, and the lymph is conveyed slowly along the channels of the cortical and medullary part towards the hilus, taking up many lymph-corpuscles in its passage. At the hilus it is gathered up by an efferent vessel or vessels (*e.l.*) taking origin in the lymph-sinuses of the medulla.

The efferent lymphatics always contain many more lymph-corpuscles than those which enter the gland, for lymph-corpuscles are constantly being formed by mitotic division of the pre-existing cells in the glandular substance, especially in the clearer centre of each cortical nodule (*germ-centre* of Flemming); they gradually find their way into the lymph-channel.

The leucocytes of the germ-centres frequently show, in sections, peculiar darkly coloured bodies—the *stainable-bodies* of Flemming—the origin of which has not been determined.

Multinucleated giant-cells are frequently found in lymph-glands.

An artery passes into each gland at the hilus; its branches are conveyed at first along the fibrous cords, but soon become surrounded by the lymphoid cords, where they break up into capillaries (fig. 300, *d*). The blood is returned by small veins, which are conducted along the fibrous trabeculæ to the hilus.

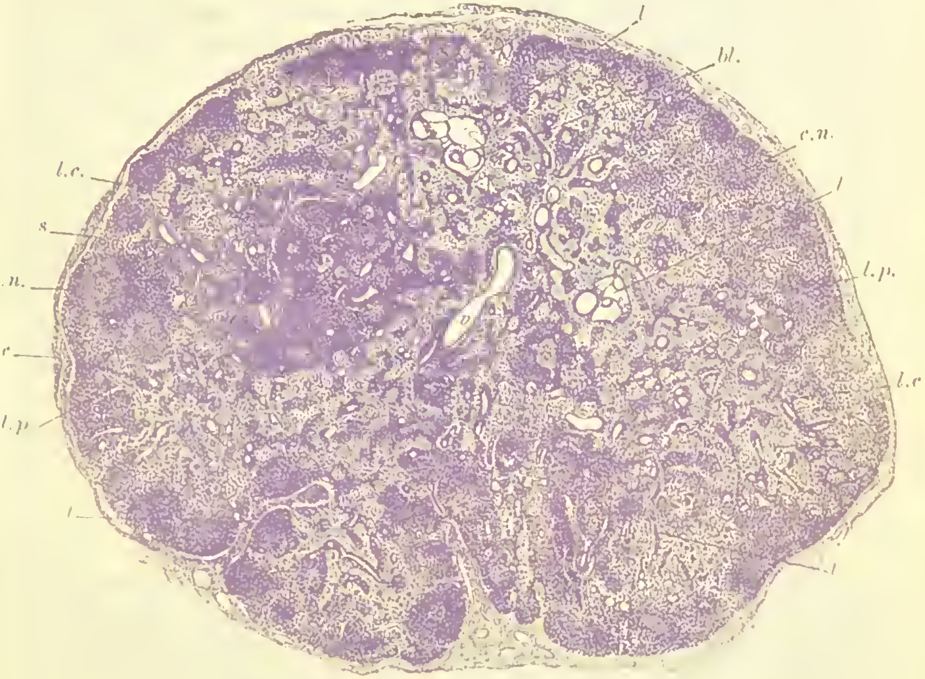

Fig. 301.—Section of a lymph-gland from the neck of an eight year old child. (v. Ebner.) × 13.

c, capsule; *c.n.*, cortical nodules, some with germ-centres; *l.c.*, lymphoid cords of medulla (dark); *l.p.*, lymph-path (light); *s*, cortical sinus; *t*, trabeculæ; *v*, vein; *l*, efferent lymph-vessels, accompanying and partly surrounding blood-vessels, *bl.*

In some lymph-glands the fibrous trabeculæ are very slightly developed, so that the gland seems in section to be almost uniformly a mass of lymphoid tissue, pervaded by lymph-channels and with clearer rounded nodules (germ-centres) scattered about, especially in the cortex (fig. 301). This is the case with most of the lymph-glands of man and some other animals. In other animals, such as the dog and ox, the trabeculæ are very well developed and contain much muscular tissue.

Nerve-fibres pass to lymph-glands and appear to be distributed chiefly as non-medullated fibres to the plain muscular tissue of the blood-vessels and trabeculæ.

Ordinary lymph-glands are confined to mammals, but Vincent and Harrison have found hæmal lymph-glands in birds.

Hæmal lymph-glands.—In many animals a certain number of lymph-glands are observable which have a red colour. Some of these on section show that what corresponds to the peripheral lymph-channel in ordinary lymph-glands is in them occupied by blood. Others have the greater part of the interior occupied by large sinuses filled with blood; but some parts have the ordinary structure of a lymph-gland. The names *hæmal glands* and *hæmal lymph-glands* (Robertson) have been given to these organs. The blood passes into the sinuses from the arterial capillaries, which probably, as in the spleen, become incomplete and open into the tissue interstices, from which at other parts the small veins in like manner arise. Like the spleen these hæmal glands show cells (phagocytes) which contain red blood-corpuscles in various stages of transformation into pigment.

Some hæmal glands are said to have no lymph-channels, but this statement requires confirmation.

The Tonsils.

The **tonsils** are two masses of lymphoid tissue placed one on each side of the pharynx, into which they project. They are covered on the free surface with the stratified epithelium of the mucous membrane, and this surface is pitted with apertures which lead into recesses or crypts in the substance of the organ (fig. 302). These recesses are all lined by a prolongation of the stratified epithelium, and into them the ducts of numerous small mucous glands open. The tonsils are composed almost entirely of lymphoid tissue, which, besides being diffused over the whole organ, is at intervals aggregated into nodules, in which the lymph-cells are more closely arranged than elsewhere. In the clear centre (*germ-centre*) of some of these nodules active multiplication of the lymph-cells by mitosis is constantly proceeding, and is, in fact, the cause of the formation of nodules in the tissue, as in other organs in which lymphoid tissue occurs. Even the epithelium which covers the tonsils is infiltrated with lymph-corpuscles (fig. 303), and these may also wander out on to the free surface, and become mingled with the saliva as salivary corpuscles.

The lymphoid tissue is highly vascular, and contains many lymphatics.

The mucous membrane of the neighbouring part of the pharynx and of the back of the tongue and that of the upper part of the pharynx near the orifices of the Eustachian tubes shows crypts

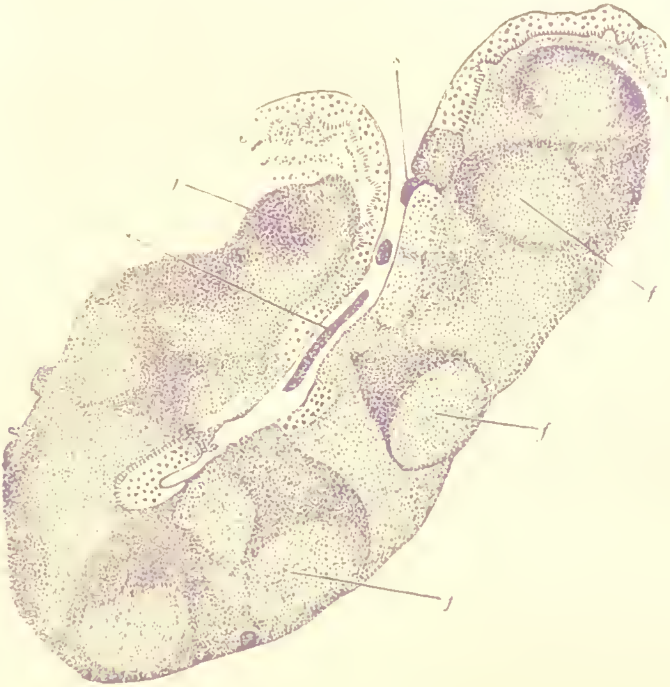

FIG. 302.—SECTION THROUGH ONE OF THE CRYPTS OF THE TONSIL. (Stöhr.)

e, *e*, stratified epithelium of surface of mucous membrane, continued into crypt; *f*, *f*, follicles or nodules of the lymphoid tissue, which is elsewhere diffuse; some show clear "germ-centres"; opposite each nodule numbers of lymph-cells are passing through the epithelium; *s*, masses of cells which have thus escaped from the organ to mix with the saliva as salivary corpuscles.

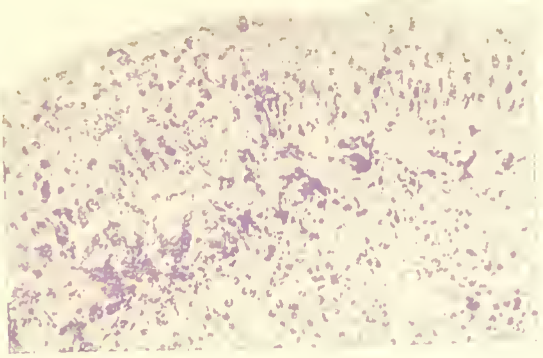

FIG. 303.—PART OF A SECTION OF RABBIT'S TONSIL SHOWING INFILTRATION OF THE EPITHELIUM BY LEUCOCYTES. Magnified 66 diameters. Photograph.

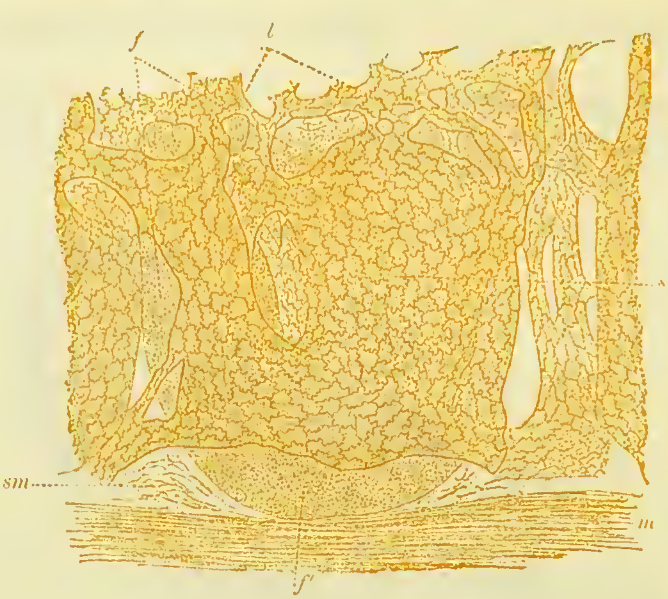

FIG. 304.—LYMPHATICS OF A PEYER'S PATCH, INJECTED WITH SILVER NITRATE: CAT. (Kölliker.) Magnified 85 diameters.

f, a lymphoid nodule or follicle; *f′*, its base, resting upon the muscular coat, *m*; *sm*, submucosa; *l*, lymph-vessels; *s*, sinus-like enlargement of lymph-vessel surrounding follicle.

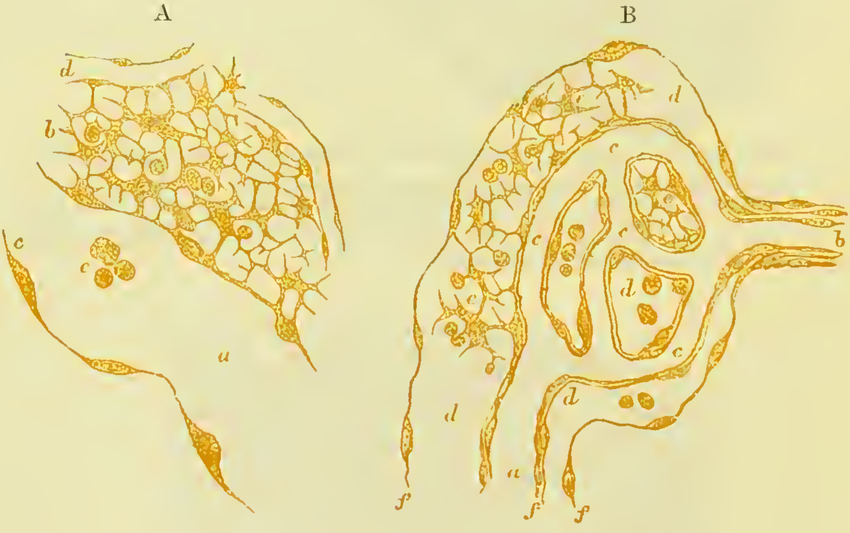

FIG. 305.—DEVELOPING LYMPHOID NODULES FROM THE GUINEA-PIG'S OMENTUM. (Klein.)

A, perilymphatic nodule; *a*, lymphatic; *c*, its endothelium; *c*, lymph-corpuscles; *b*, accumulation of lymphoid tissue on one side of it; *d*, blood-capillaries within this.

B, endolymphatic nodule consisting of an enlarged lymphatic vessel, *d*, within which is a capillary network, *c*, *c*, an artery, *b*, and a vein, *a*; *c*, lymphoid tissue within the lymphatic, its branched cells being joined to and derived from the lymphatic endothelium, *f*.

and masses of lymphoid or adenoid tissue similar in structure to those of the tonsils.

OTHER LYMPHOID STRUCTURES.

Lymphoid tissue occurs in many other parts of the body in addition to the lymphatic glands and tonsils, although it may not, as in these structures, constitute the bulk of the organ. Thus it is found in many mucous membranes, such as those of the intestine and of the respiratory tract, both in a diffuse form and also collected into nodular masses which are like the cortical nodules of a lymph-gland, and may, like these, be partially surrounded by a lymph-sinus. In the intestine such nodules constitute the so-called *solitary glands* and *Peyer's patches.* The lymphatics form plexuses of sinus-like vessels which to a large extent inclose the nodules (fig. 304). In the spleen a large amount of lymphoid tissue is found ensheathing the smaller arteries, and also expanded into nodular masses (*Malpighian corpuscles of the spleen*). All these structures will be studied subsequently. Lymphoid tissue also occurs in considerable amount in the serous membranes, especially in young animals; in the adult it is here mostly replaced by adipose tissue.

Development of lymphoid tissue.—Lymph-glands are developed in connection with plexuses of lymph-vessels, an accumulation of retiform tissue and lymph-cells taking place either external to and around the lymphatics (*perilymphatic formation*) ; or some of the lymphatics are dilated into a sinus or sinuses and the formation of the lymphoid tissue occurs within it (*endolymphatic formation*) (fig. 305, A and B). When there is a development of lymphoid tissue outside the lymphatic vessels this may form a considerable accumulation before the formation of lymph-paths within the tissue. Blood-vessels are early developed amongst the lymphatic plexuses, and by these, according to Gulland, the first lymph-corpuscles of the lymphoid tissue are brought to the gland.

The marginal sinus is produced by the fusion of a number of lymph-vessels which surround the accumulation of lymphoid tissue, while in the situation of the future hilus other lymph-vessels grow into the glandular substance and form channels which subdivide it up into cords and nodules (Kling). The branched cells of the lymph-path are said to be derived from the lymphatic endothelium.

The axillary glands were found by Stiles to increase in number and size during lactation, diminishing again after lactation has ceased. In the developing tonsils Gulland occasionally found nests of epithelial cells detached from the surface epithelium, somewhat like those found permanently in the thymus.

THYMUS.

The **thymus gland** is an organ which in man is found only in the embryo and during infancy. It is composed of a number of lobules (figs. 306, 307) varying in size, which are separated from one another by septa of connective tissue, along which the blood-vessels and lymphatics pass to and from the lobules. Each lobule shows plainly, when examined with a low power, a distinction into an outer cortical and an inner medullary portion. The cortical part of the lobule is imperfectly divided into nodules by trabeculæ of connective tissue. It is highly vascular, and is superficially similar in structure to the lymphoid tissue of the lymph-glands and tonsils, with which it also agrees in exhibiting numerous indications of indirect cell-division, but without definite germ-centres. Besides lymph-corpuscles it contains a number of peculiar granular cells. The medulla is more open in its texture, and its reticulum is formed by large, transparent, branched cells (fig. 308), which are sometimes massed together and then resemble epithelium-cells. The medulla contains fewer lymph-corpuscles than the cortex and has a clearer aspect. Connective-tissue fibres are not wholly absent from it. Within the medulla, but not in the cortex, are found peculiar concentrically striated bodies (the *concentric corpuscles of Hassal*, figs. 307, 309), which are "nests" of flattened epithelial cells arranged concentrically around one or more central cells, which have often undergone a degenerative process. Sometimes these corpuscles are compound, two or three being grouped together and similarly inclosed by flattened cells. They represent part of the remains of an epithelial tube, which forms the thymus rudiment of the early embryo and is derived from certain of the branchial clefts. According to the observations of Hammar the reticulum of the gland is also derived from this epithelium, and Stöhr believes that the apparent lymphoid cells of the gland have a similar origin.

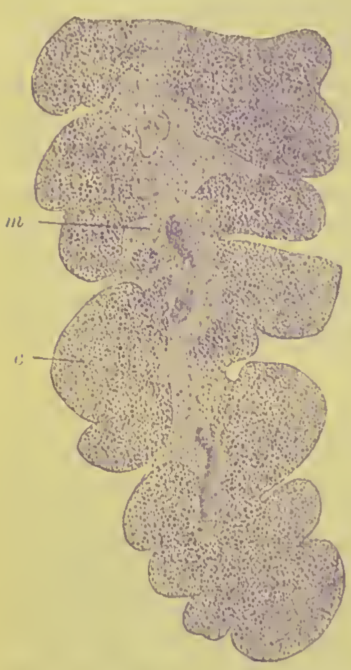

FIG. 306.—SECTION OF DEVELOPING THYMUS. (From Prenant, Bouin, and Maillard.)

c, cortex; *m*, medulla. At this period the medulla is continuous throughout the gland, and comes to the surface at places.

Nucleated red blood-corpuscles (erythroblasts), similar to those found in red marrow, have also been described in the thymus (J. Schaffer), and occasionally cysts lined by ciliated epithelium are found (fig. 309, *c*).

In some animals islands of striated muscular cells are seen in the medulla. Multinucleated giant-cells are also found (Watney).

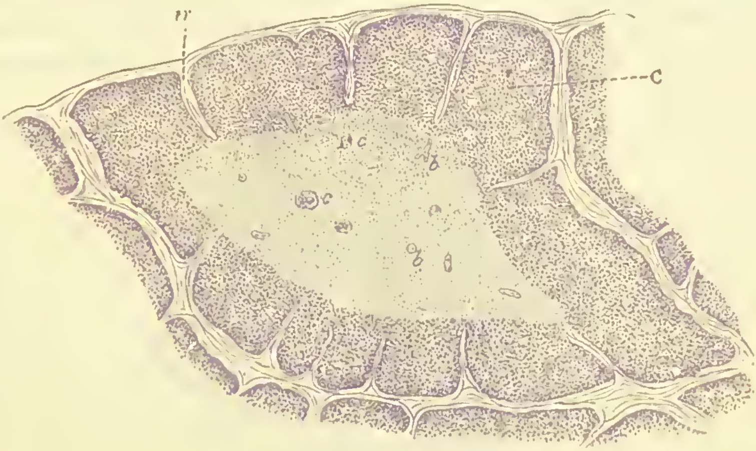

FIG. 307.—A LOBULE OF THE THYMUS OF A CHILD, AS SEEN UNDER A LOW POWER. c, cortex ; *c*, concentric corpuscles within medulla ; *b*, blood-vessels ; *tr*, trabeculæ.

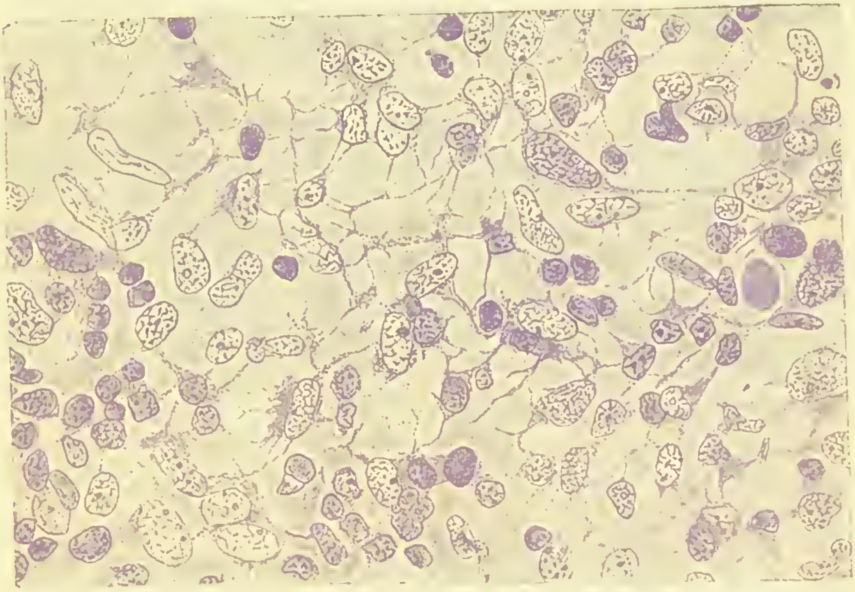

FIG. 308.—SECTION OF MEDULLA OF THYMUS, SHOWING BRANCHED (EPITHELIAL) CELLS OF RETICULUM AND A CERTAIN NUMBER OF LYMPHOID CELLS IN THE MESHES. (Hammar.)

The lobules, the cortex especially, are abundantly supplied with capillary blood-vessels. In man the arteries penetrate to the junction of cortex and medulla, and give off most of their capillaries radially into the cortical nodules. Veins pass away both from the surface of the lobules and to a less extent directly from the medulla. The mode of distribution of the lymphatics has not been definitely ascertained, but none are seen within the lobules. Nevertheless, large lymphatic vessels, containing many lymphocytes, issue from the interstitial connective tissue of the thymus, but in what way they are connected with the lobules has not been ascertained.

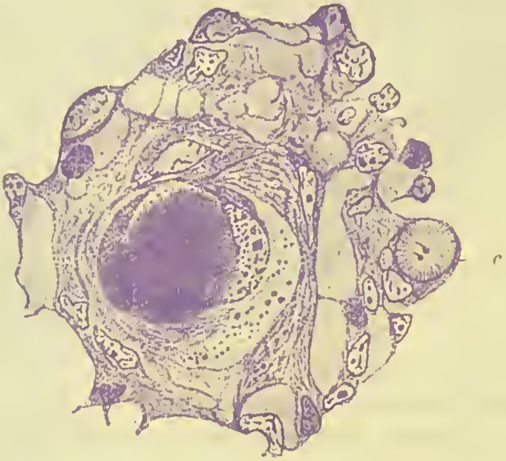

FIG. 309.—A CONCENTRIC CORPUSCLE OF THYMUS WITH PART OF THE ADJOINING RETICULUM. (Hammar.)
c, a small ciliated cyst.

In the human subject the thymus gland undergoes after childhood a process of retrogression, its lobules ceasing to grow and becoming surrounded and concealed by a quantity of adipose tissue which develops in the interstitial connective tissue of the gland. Eventually the lobules atrophy.

LESSON XXIII.

STRUCTURE OF THE SPLEEN, SUPRARENAL CAPSULES, THYROID BODY, AND PITUITARY BODY.

1. SECTIONS of the spleen hardened in Müller's fluid or formol and stained with hæmatoxylin and eosin. Notice the trabeculæ extending into the substance of the organ from the capsule. Notice also that the glandular substance is of two kinds, (1) lymphoid tissue accumulated around the small arteries and here and there massed to form *lymphoid nodules*—the Malpighian corpuscles—and (2) a tissue—the red pulp—consisting of a reticulum of fibrils and branching cells: this tissue contains blood in its interstices.

Sketch part of a section under a low power and a small portion of the pulp under a high power.

2. Sections across a suprarenal capsule hardened in 2 per cent. bichromate of potassium. In sections not otherwise stained, notice the deep brown coloration of the medulla (action of the chromic salt). Stain other sections with eosin and hæmatoxylin. Examine first with a low power, noticing the general arrangement and extent of the cortical and medullary parts of the organ, and making a general sketch which shall include both. Afterwards sketch carefully under the high power a group of cells from each part of the organ.

3. Sections of the thyroid body stained with eosin and hæmatoxylin. Notice the vesicles lined with cubical epithelium and filled with a "colloid" substance which becomes stained with hæmatoxylin. Sketch one or two vesicles. Measure several vesicles. The sections should include a parathyroid.

4. Sections (antero-posterior) through the pituitary body. Notice the (epithelial) anterior lobe separated by a cleft from the (nervous) posterior lobe. The anterior part of the posterior lobe is also covered by an epithelial layer, amongst the cells of which colloid matter may be seen. This also can be traced in the tissue of the posterior lobe as far as the infundibulum of the third ventricle.

5. Injected preparations of these organs may also be studied: the spleen is usually naturally injected with blood.

THE SPLEEN.

The **spleen** is the largest of the so-called ductless glands. It appears to be functionally connected with the blood, white blood-corpuscles being formed and coloured blood-corpuscles being submitted to destruction within it.

Like the lymph-glands, the spleen is invested with a fibrous and muscular *capsule* (fig. 310), which is, however, stronger and has far more plain muscular tissue; outside the capsule is a covering derived from the serous membrane. The capsule sends bands of trabeculæ into the organ (fig. 311), and these join with a network of similar trabeculæ which pass into the gland at the hilus along with the blood-vessels. In the interstices of the framework thus constituted lies a soft pulpy substance containing a large amount of blood, and therefore of a deep red colour, dotted within which are here and there to be seen small round bodies, whiter than the pulp in the fresh organ but darker in stained sections, the *Malpighian corpuscles* of the spleen. These are composed of lymphoid tissue which is gathered up into masses which envelop the smaller arteries, whilst the red pulp which everywhere surrounds them and which forms the bulk of the organ is composed (Carlier) of a close network of connective-tissue fibrils (fig. 312), partly covered by flattened and branched cells (fig. 313). Passing into the pulp and communicating with its interstices are capillary blood-vessels which are connected with the terminations of the arteries; whilst in other parts venous channels—characterised in the human spleen by an encirclement of reticulum-fibres, possibly of an elastic nature (fig. 314), and by the presence of a layer of highly

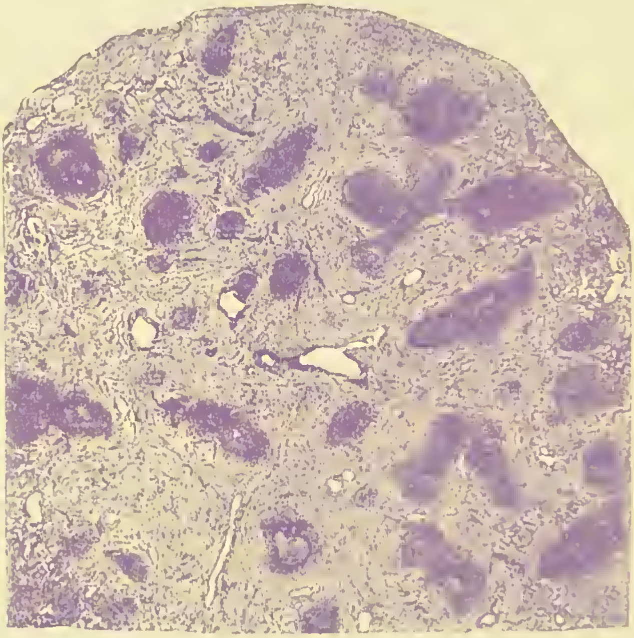

FIG. 310.—SECTION OF SPLEEN, SOMEWHAT MAGNIFIED. (G. Mann.)

The section was stained, and the Malpighian corpuscles therefore appear darker than the pulp. The venous sinuses show as clear spaces. The larger veins are contained in the trabeculæ.

characteristic, comparatively thick and prominent endothelium-cells (fig. 315)—course through the pulp and bring the blood which has passed into its interstices from the arterial capillaries towards the larger veins of the organ, which run in the trabeculæ, and are by them conducted to the hilus. The arteries, which are also at first conducted from the hilus along the trabeculæ into the interior of the organ, presently leave the trabeculæ, and their external coat becomes gradually converted into a thick sheath of lymphoid tissue which invests them in the remainder of their course, and in places becomes swollen into the Malpighian corpuscles already mentioned. The small arteries distribute a few capillaries to the Malpighian corpuscles, and then break up into pencils of capillary vessels which open into the interstices of the pulp.

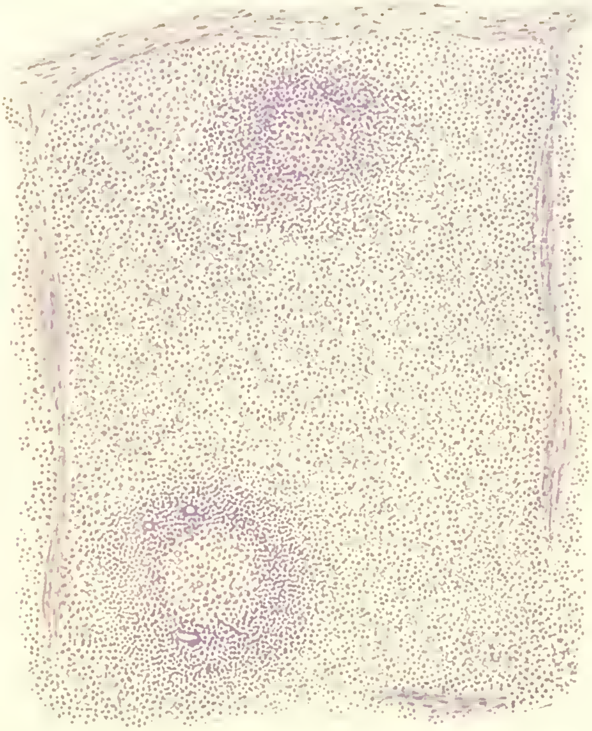

FIG. 311.—VERTICAL SECTION OF A PORTION OF THE MONKEY'S SPLEEN, AS SEEN WITH A LOW POWER.

The Malpighian corpuscles frequently but not always show a clearer central nodule or *germ-centre*, characterised by the presence of numerous mitoses; and the stainable bodies of Flemming (p. 235) are also seen in them.

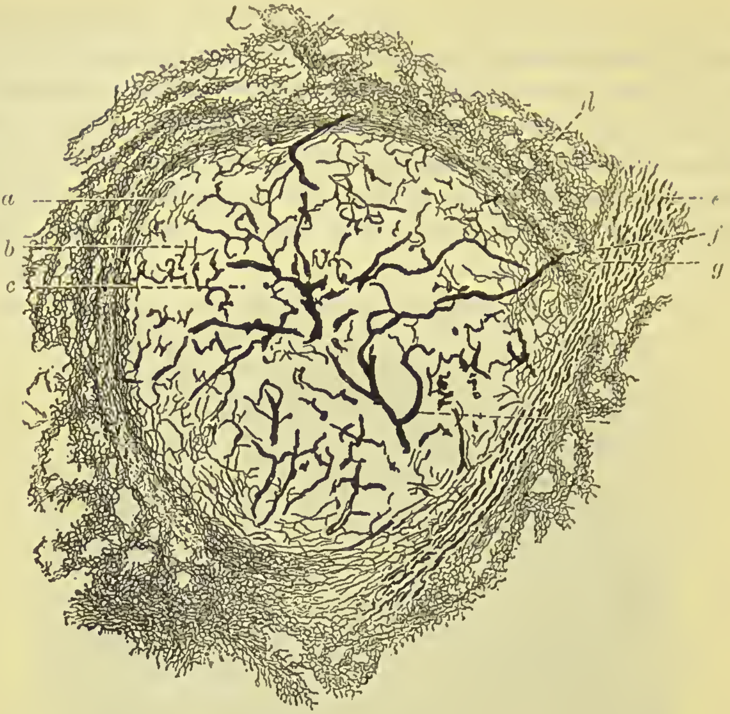

FIG. 312.—RETICULUM OF SPLEEN, GOLGI METHOD. (Oppel.)
a, Malpighian corpuscle; *b*, part of its reticulum; *c*, condensed reticulum at its margin; *d*, more open tissue next to this; *e*, wall of arteriole; *f*, capillaries of Malpighian corpuscle; *g*, reticulum of arteriole expanding into that of the Malpighian corpuscle.

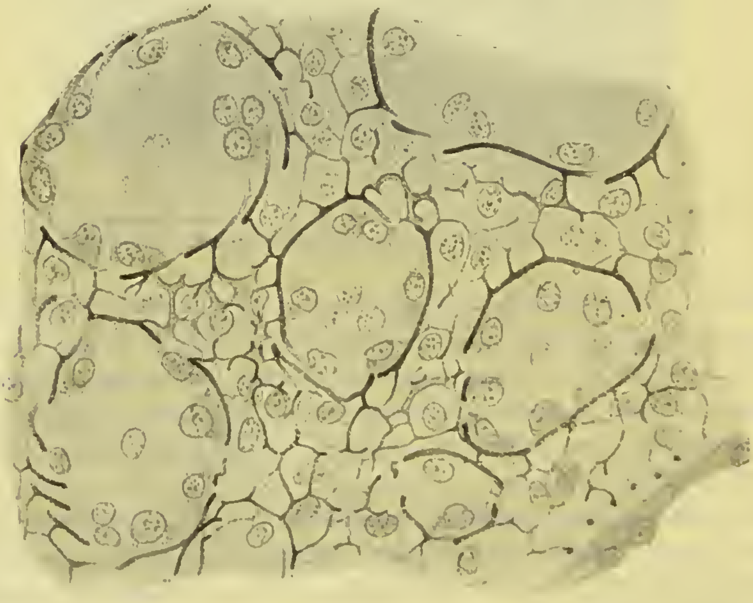

FIG. 313.—SMALL VEINS OF SPLEEN PULP WITH RETICULAR TISSUE. (Hoyer.)
The veins, which are invested by encircling fibres, show gaps in their walls whereby they communicate with the interstices of the pulp.

Some authorities hold that the arterial capillaries open into the venous sinuses, and that the blood-system of the spleen is therefore a closed one, the blood-corpuscles passing into the pulp-interstices by diapedesis.

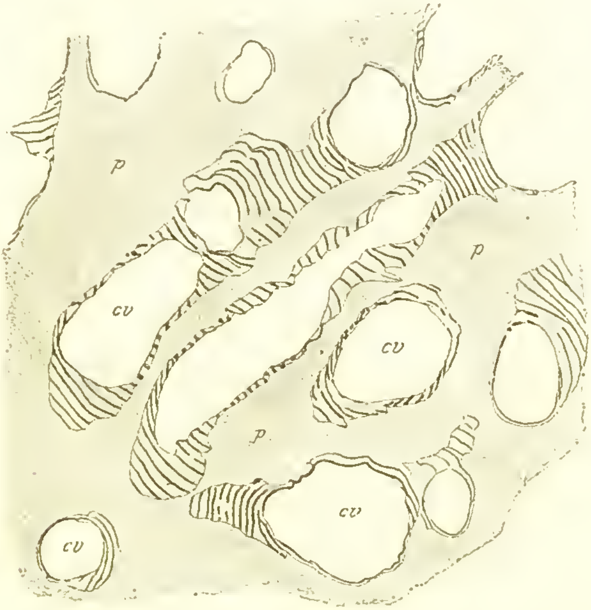

FIG. 314.—VENOUS SPACES OF SPLEEN PULP, SHOWING THE ENCIRCLING FIBRES IN THEIR WALLS: HUMAN. (v. Ebner.)

cv, capillary veins; *p*, pulp (the tissue elements are not represented).

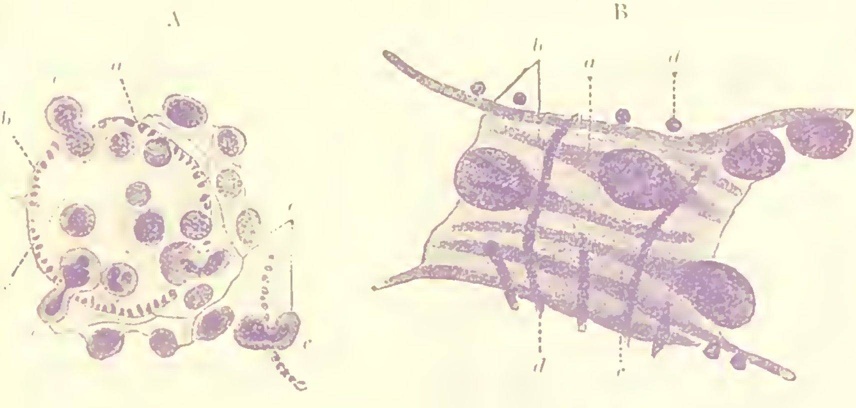

FIG. 315.—FROM SECTIONS OF HUMAN SPLEEN. (Weidenreich.)

A, transverse sections of a venous sinus. B, longitudinal section of a smaller sinus considerably more magnified than A.

a, nucleated bodies of endothelial cells; *b*, fibre-like prolongations of endothelial cells; *c*, cavity of sinus; *d*, encircling elastic fibres; *e*, *e*, leucocytes passing through wall of sinus.

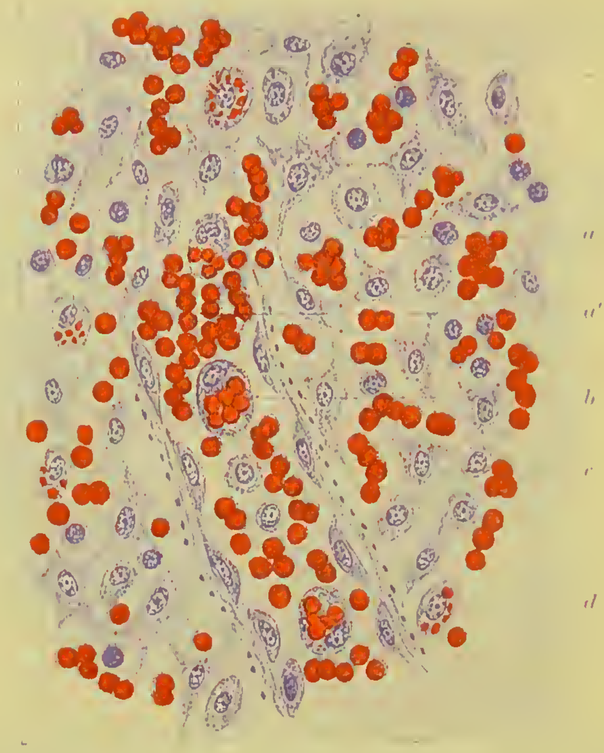

FIG. 316.—THIN SECTION OF SPLEEN-PULP OF CHILD, HIGHLY MAGNIFIED, SHOWING THE APPARENT MODE OF ORIGIN OF A SMALL VEIN IN THE INTERSTICES OF THE PULP. Magnified 400 diameters.

a, blood in pulp; *a'*, blood in vein; *b*, phagocyte in vein; *c*, branched cell of pulp; *d*, phagocytic splenic cell.

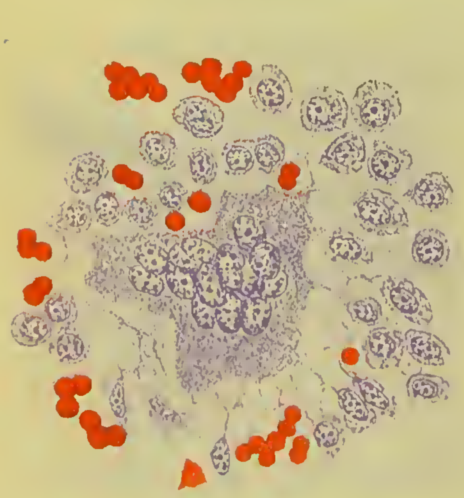

FIG. 317.—A GIANT CELL FROM THE SPLEEN OF A KITTEN. Magnified 400 diameters.

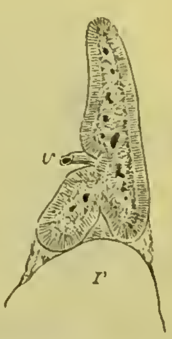

FIG. 318.—A VERTICAL SECTION OF THE SUPRARENAL BODY OF A FŒTUS, TWICE THE NATURAL SIZE, SHOWING THE DISTINCTION BETWEEN THE MEDULLARY AND CORTICAL SUBSTANCE. (A. Thomson.)

v, issuing vein: *r*, summit of kidney.

The special cellular elements of the spleen-pulp are of three kinds, viz. (1) large, amœboid phagocytic *splenic cells*, (2) *giant cells*, (3) branched *reticulum-cells* which assist in forming the sponge-work. The pulp also contains all the corpuscular elements of blood. The phagocytic cells are frequently found to contain coloured blood-corpuscles in their interior in various stages of transformation into pigment. They occur both in the interstices of the pulp and in the venous sinuses and veins, where they are often filled with erythrocytes (fig. 316). The giant cells are most frequent in young animals (fig. 317). The branched cells of the sponge-work are probably of the same nature as the endothelium cells of the terminal capillaries and veins of the pulp. They are connected with one another and with the endothelial cells of the small vessels by branches. The phagocytic spleen cells are perhaps derived from them.

Nucleated coloured corpuscles are found in the embryo, and occasionally after birth, in the spleen-pulp. The blood of the splenic vein is very rich in leucocytes.

The lymphatics of the spleen run partly in the trabeculæ and capsule, and partly in the lymphoid tissue ensheathing the arteries. They join to form larger vessels which emerge together at the hilus. There are no lymphatics in the spleen-pulp.

The nerves, which are numerous and mostly non-medullated, are distributed to the muscular tissue of the arteries and to that in the capsule and trabeculæ.

Mall states that the distribution of the trabeculæ and of the blood-vessels within the spleen is such as to indicate a differentiation of the pulp into divisions which he terms "spleen lobules," each of which has its own arteriole and venule, and in which the pulp is arranged in columns or cords surrounded by venous spaces. It must, however, be understood that there is nothing of the nature of partitions separating such lobules ; to all appearance the pulp is in continuity throughout the organ.

THE SUPRARENAL CAPSULES.

The **suprarenal capsules** (adrenals) belong to the class of bodies known as ductless glands, but they are entirely different in structure and function from the spleen and lymphatic glands. A section through the fresh organ (fig. 318) shows a *cortex* which is striated vertically to the surface, and of a yellowish colour, and a *medulla* which is soft and highly vascular, and of a dark-red colour. The whole organ is invested by a fibrous *capsule* which sends fibrous septa inwards through the cortical substance (fig. 319), subdividing this for the most part into columnar groups of cells (*zona fasciculata*, *c*). Immediately underneath the capsule, however, the groups are more rounded, and the cells tend to assume a columnar form (*zona glomerulosa*, *b*), whilst next to the medulla they have a reticular arrangement (*zona reticularis*, *d*).

The cells which form the cortical substance are, for the most part, polyhedral in form; each contains a clear round nucleus, and there are often yellowish oil-globules in their protoplasm. No arteries and veins penetrate between these cells, both these and the lymphatics of the cortex running in the fibrous septa between the columns of cells, which they surround with a capillary network. In the zona reticularis the capillaries widen out and occupy the spaces between the cell-columns (fig. 319, *d*). The lymphatics communicate with fine canals between the cells of the cortex.

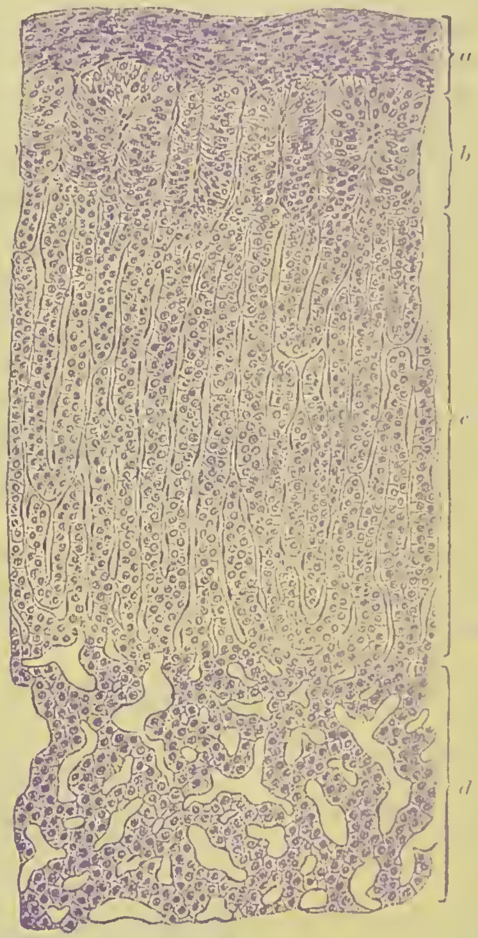

FIG. 319.—VERTICAL SECTION OF CORTEX OF SUPRARENAL OF DOG. (Böhm and v. Davidoff.) Magnified about 150 diameters.

a, capsule; *b*, zona glomerulosa; *c*, zona fasciculata; *d*, zona reticularis.

The cells of the medulla (fig. 320) are more irregularly disposed. They are supported by a network of elastic fibres. They lie in very close relation to the large capillary blood-spaces (sinusoids) which pervade the medulla, and they probably pour a secretion directly into the blood. Their protoplasm is granular; in some animals it contains a brownish pigment, but in man the dark-red colour of the medulla is due to the blood contained in the large sinusoid spaces by which it is pervaded, and which receive the blood after it has traversed the capillaries of the cortex. A few arterioles pass straight to the medulla through the cortex. One large vein usually passes out at

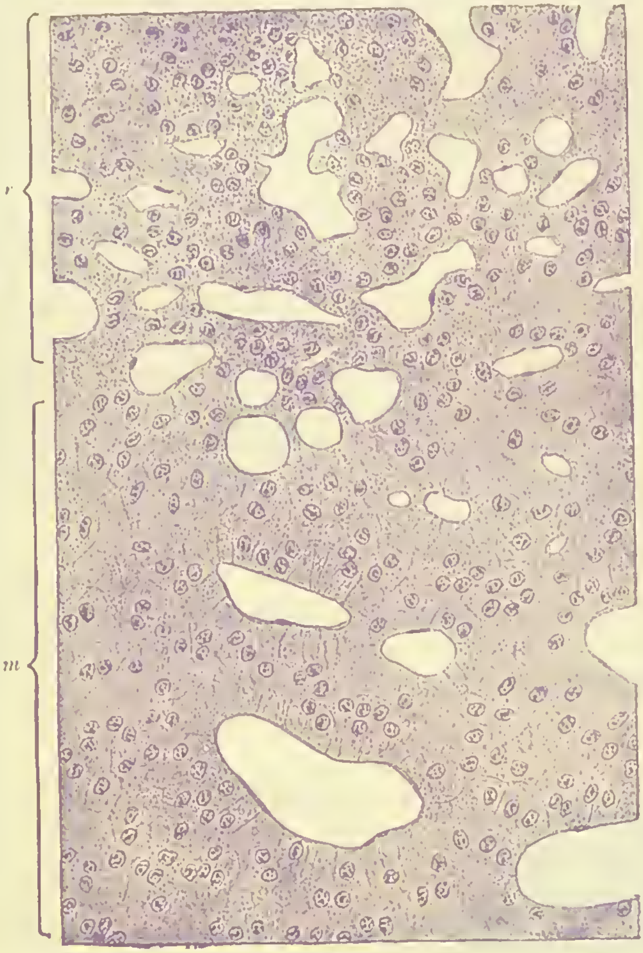

Fig. 320.—Section showing zona reticularis of cortex, *r*, and medulla, *m*, of suprarenal of dog. (Szymonowicz.) Magnified 384 diameters.

the hilus in the anterior surface of the gland. Investing the larger veins are longitudinal bundles of plain muscular fibres; but most of the veins have only an endothelium. Numerous nerves, after traversing the cortical substance, are distributed throughout the medulla, where they form a close plexus provided here and there with ganglion-cells. The cells of the medulla are characterised by staining brown by chromic acid and its salts, provided the organ is fresh (chromophil or chromaffin cells). A similar staining reaction is found to occur in some of the cells of certain small glandular bodies which occur irregularly at the back of the abdomen, being especially frequent near the lower end of the aorta (fig. 321).

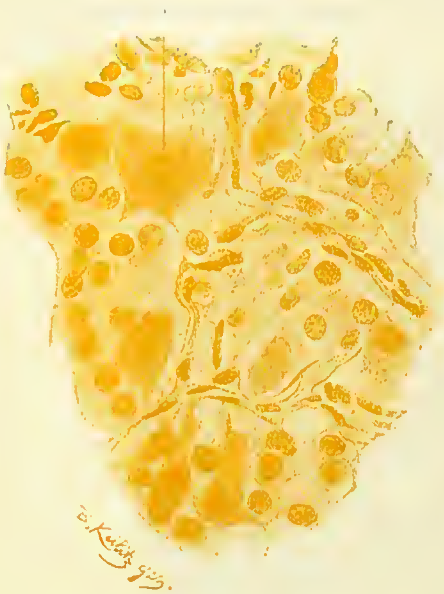

FIG. 321.—SECTION OF PART OF AN ACCESSORY SUPRARENAL (CHROMOPHIL) BODY; NEW-BORN CHILD. (Zuckerkandl.)

The medulla of the suprarenal capsule is developed from cells which become detached from the rudiments of the sympathetic ganglia, and are therefore of ectodermal origin. The cortex is developed from mesoderm.

THE THYROID BODY.

The **thyroid body** consists of a framework of connective tissue inclosing numerous spherical or oval vesicles (fig. 322) which are lined with cubical epithelium-cells; these often contain granules of a fatty character. The cavities of the vesicles are usually occupied by a peculiar viscid liquid (colloid) which is coagulated by alcohol and which then becomes stained with hæmatoxylin. A similar material has been found in the lymphatics of the gland, and may often be detected also in the interstices of the connective tissue. The amount of colloid in the vesicles varies considerably in different individuals; the circumstances which influence its variations are not fully understood, but diet appears to play an important part (Chalmers Watson).

The blood-vessels of the thyroid are numerous. The capillaries form close plexuses round the vesicles (fig. 323), and even extend between the lining epithelium cells.

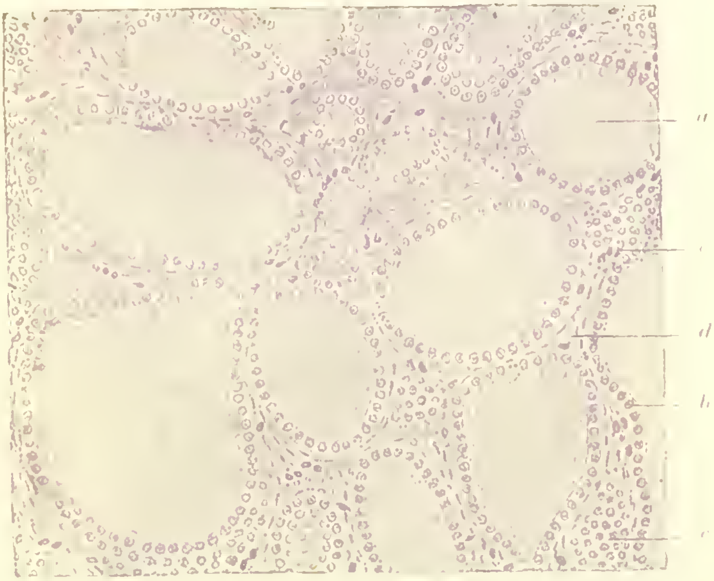

Fig. 322.—Section of human thyroid. (Szymonowicz.) Magnified about 180 diameters.

a, vesicle occupied by colloid, which has partly shrunk away from the epithelium; *b*, epithelium of a large vesicle; *c*, *c*, epithelium of vesicles which are cut tangentially; *d*, interstitial connective tissue.

The thyroid is originally formed, like an ordinary gland, by an outgrowth from the buccal epithelium; later, the connection becomes severed and its branching tubules are broken up into isolated vesicles.

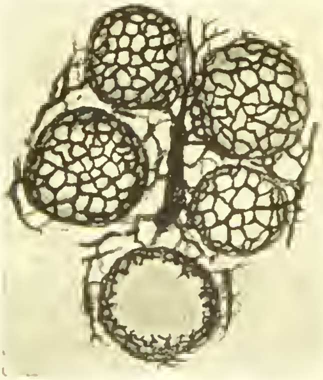

Fig. 323.—Thyroid of dog injected.

Parathyroids.—In close proximity to or embedded in the substance of the thyroid are always to be found four small glandular organs of different structure from the thyroid proper (fig. 324). These bodies, one of which usually lies on the lateral and one on the mesial surface of each lateral lobe, are formed of columns of granular epithelium-cells, with numerous blood-channels between the columns. If left after removal of the thyroid, the parathyroids are stated to undergo hypertrophy, and to develop a vesicular structure (Vincent and Jolly). There is also frequently to be found in connection with the thyroid a small mass of lymphoid tissue which resembles the thymus tissue in structure, and, like it, contains concentric corpuscles.

CAROTID AND COCCYGEAL GLANDS.

These are minute glandular organs without ducts, lying respectively at the bifurcation of the carotid artery and in front of the apex of the coccyx. They are composed of polyhedral cells, with numerous blood-capillaries between them. In the carotid gland the cells are collected into spheroidal clumps (fig. 325), in the coccygeal gland into irregular nodules (fig. 326). The blood-vessels, at least in the coccygeal gland, have a sinusoidal character (Walker). Amongst the cells are some which stain dark brown with chromic acid like those of the medulla of the suprarenal capsules (chromophil cells). A certain number of such cells occur also, according to Kohn, in some sympathetic ganglia.

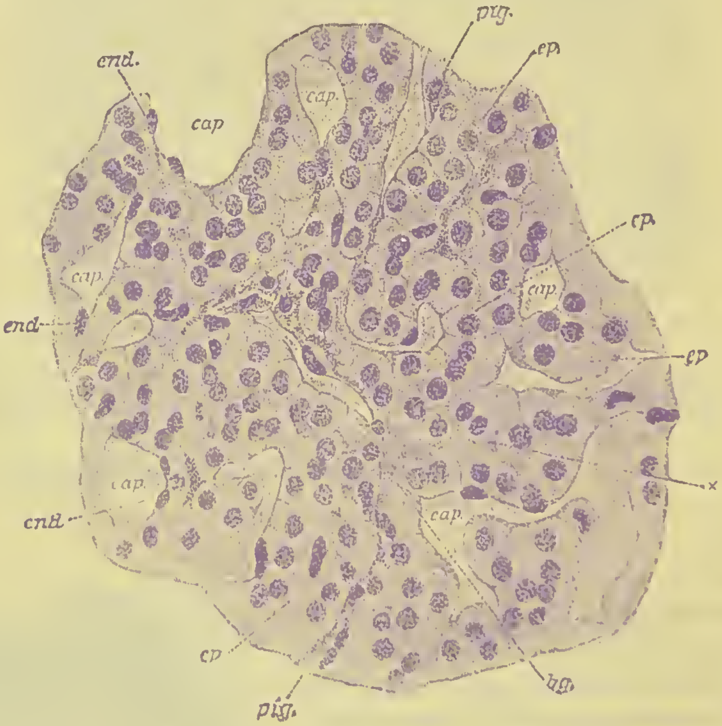

FIG. 324.—SECTION OF PARATHYROID. (Kohn.)
ep, secreting epithelium; *pig*, cells containing pigment; *cap*, sinus-like capillaries; *end*, endothelium-cells.

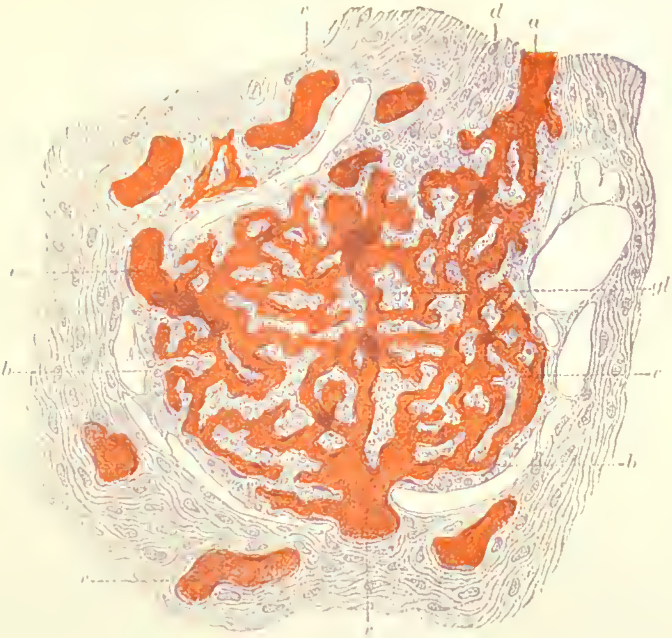

FIG. 325.—A CLUMP OR CELL-BALL FROM THE CAROTID GLAND, INJECTED. (Schaper.)

a, arteriole; *v*, venules; *c*, sinus-like capillary within nodule; *gl*, group of gland cells; *c*, boundary of nodule surrounded by lymph space; *d*, inter-nodular connective tissue of gland.

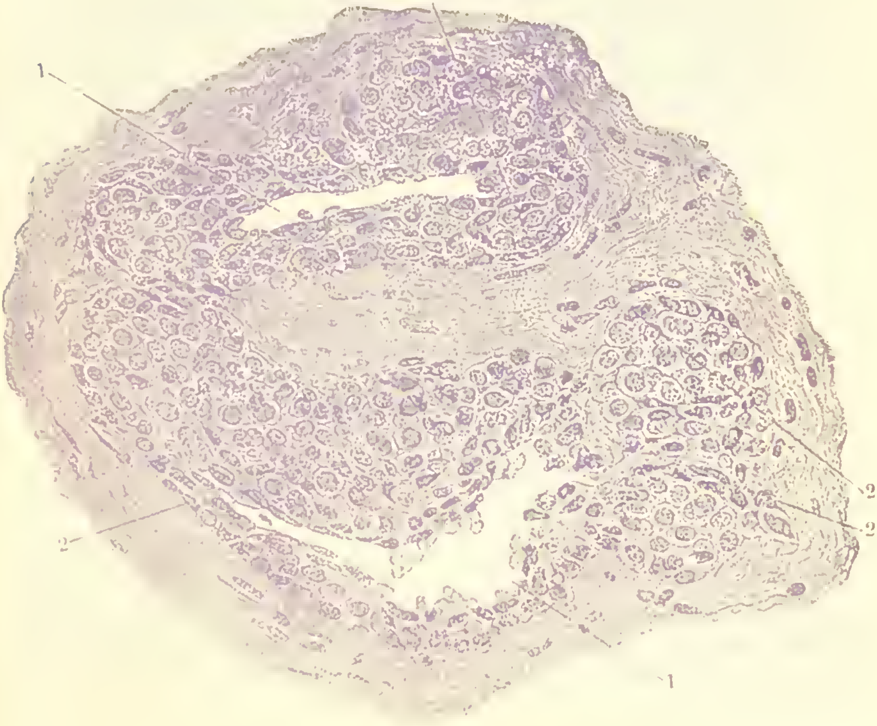

FIG. 326.—SECTION OF COCCYGEAL GLAND. (Walker.)

1, blood-spaces; 2, epithelium; 3, connective tissue.

THE PITUITARY BODY.

The **pituitary body or gland** (*hypophysis cerebri*) is a small reddish mass which lies in the sella turcica, and is connected with the third ventricle by the infundibulum. It consists of three parts, a larger anterior and a smaller posterior, with an intermediate part between them. Between the anterior and intermediate parts there is usually a cleft-like space containing glairy fluid (fig. 327). The *anterior* part is originally developed as a hollow protrusion of the buccal epithelium. It consists at first of a number of tubules, which are lined by epithelium and united by connective tissue, but for the most part the lumen of the tubules has become obliterated in the adult, and they present the appearance of solid cell-masses between which are numerous large venous capillaries, perhaps sinusoids. Some of the cells are clear, others darkly granular in appearance (figs. 327, 328).

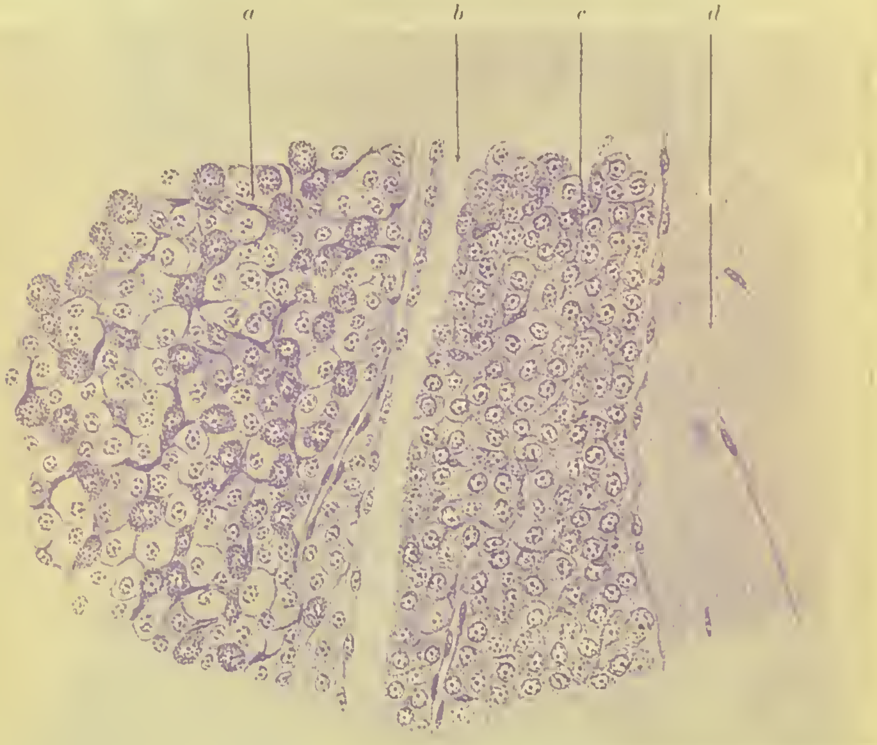

FIG. 327.—SECTION OF CAT'S PITUITARY PASSING THROUGH THE CLEFT IN THE GLAND. (P. T. Herring.)

a, pars anterior; *b*, cleft; *c*, pars intermedia; *d*, pars posterior; seu nervosa.

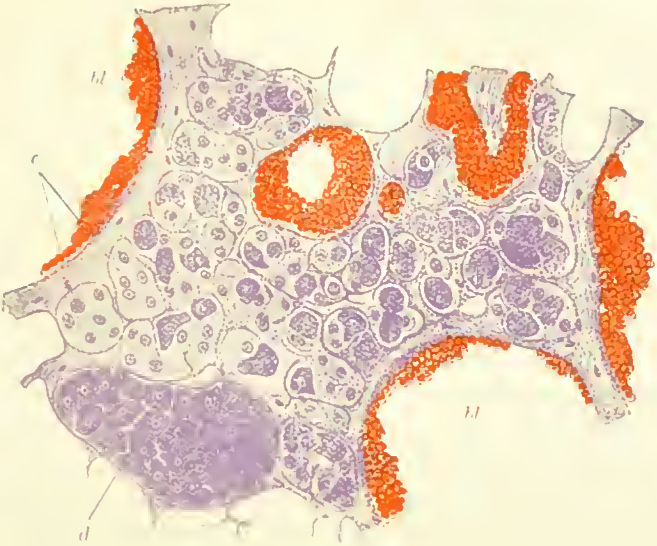

FIG. 328.—SECTION OF ANTERIOR LOBE OF HYPOPHYSIS OF OX. (Dostoiewsky.)

bl, blood-sinuses; *c*, cell-strands containing clear cells; *d*, strands of darker granular cells. Other strands contain both kinds of cell.

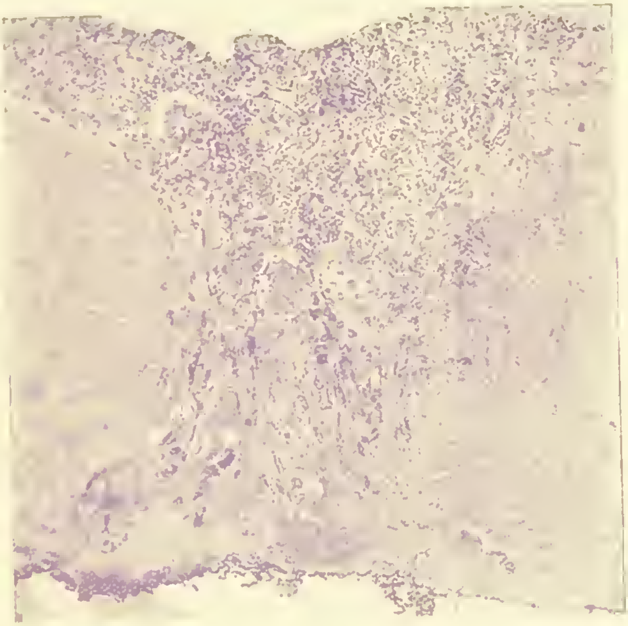

FIG. 329.—SECTION OF PART OF PARS INTERMEDIA AND PARS POSTERIOR OF DOG EXTENDING FROM THE GLANDULAR CLEFT (BELOW) TO THE INFUNDIBULAR CAVITY (ABOVE). (P. T. Herring.)

The section shows the colloid matter which is formed in cells of the pars intermedia passing towards the infundibulum of the third ventricle. The amount of colloid has been increased as the result of removal of the thyroid nineteen days earlier.

The intermediate part is formed of clear cells only, and is much less vascular than the anterior part. Its cells tend to undergo a transformation into a sort of "colloid" material; a mass of colloid being sometimes surrounded by untransformed cells, and thus presenting a superficial resemblance to a vesicle of the thyroid body. The colloid when formed passes through the tissue of the posterior part of the organ, and eventually becomes set free into the extension of the third ventricle which projects downwards into the base of the pituitary body (Herring).

The colloid is increased after thyroidectomy, but does not contain organically combined iodine as does the colloid of the thyroid itself.

The *posterior* part of the pituitary body, which is developed from the infundibulum of the third ventricle, consists chiefly of neuroglia. In man the posterior lobe is stated to contain no cells in the adult of distinctly nervous character, but it receives nerve-fibres which arise from large cells in the grey matter just behind the optic chiasma; some of these fibres penetrate into the glandular substance.

LESSONS XXIV. AND XXV.

THE SKIN.

1. Sections of skin from the palmar surface of the fingers. The skin is hardened in picric acid or formol, followed by alcohol. The sections are made vertical to the surface, and should extend down as far as the subcutaneous tissue. Notice the layers of the epidermis and their different behaviour to staining fluids. Notice also the papillæ projecting from the corium into the epidermis and look for tactile corpuscles within them. In very thin parts of the sections the fine intercellular channels in the deeper parts of the epithelium (see Lesson VII.) may be seen with a high power. The convoluted tubes of the sweat-glands are visible here and there in the deeper parts of the corium, and in thick sections the corkscrew-like channels by which the sweat is conducted through the epidermis may also be observed. Make a sketch showing the general structure under a low power, and other sketches to exhibit the most important details under a high power. Measure the thickness of the epidermis and the length of the papillæ.

2. Sections of the skin of the scalp, vertical to the surface and parallel to the slope of the hair-follicles, and others parallel to the surface, and therefore across the hair-follicles. Stain and mount in the same way as in the last preparation. Examine also the structure of the hairs.

In these preparations the details of structure of the hair and hair-follicles, together with the sebaceous glands and the little muscles of the hair-follicles, are to be made out.

3. Vertical sections of the nail and nail-bed. To cut such hard structures as the nail it is best, after fixing with picric acid or formol followed by 75 p.c. alcohol, to soak the tissue in strong gum arabic for a few days, then place it in an appropriate position upon a cork or upon the object-carrier of a microtome, and plunge the whole into 70 per cent. alcohol. This renders the gum hard, and enables sections to be cut of sufficient fineness. A plane iron should be used with the microtome, since the hardness of the nail will turn the edge of a razor. To remove the gum the sections are placed in water for a few hours; they may then be stained and mounted. Notice the ridges (not papillæ) of the corium, projecting into the epidermis. Observe also the distinction of the epidermis into Malpighian layer and nail proper.

4. Mount a section from a portion of skin in which the blood-vessels have been injected, and notice the distribution of the capillaries to the sweat-glands, to the hair-follicles, and to the papillary surface of the corium.

5. The cells which compose the nails and hairs can be isolated by warming a small piece of nail or hair in strong sulphuric acid; after this treatment the cells are readily separated from one another by pressure upon the cover-glass.

6. Sections of mammary gland during lactation. The gland may be fixed in Zencker's fluid (see Appendix) and the sections stained with hæmatoxylin and eosin.

The skin is composed of two parts, *epidermis* and *cutis vera* (figs. 330, 331).

The **epidermis**, or scarf skin, is a stratified epithelium (fig. 332). It is composed of a number of layers of cells, the deeper of which are soft and protoplasmic, and form the *rete mucosum* of Malpighi, whilst the superficial layers are hard and horny, this horny portion sometimes constituting the greater part of the thickness of the epidermis. The deepest cells of the *rete mucosum*, which are set on the surface of the cutis vera, are columnar in shape. In the coloured races of mankind these cells contain pigment-granules. In the layers immediately above them the cells are polyhedral. Between all these cells of the rete mucosum there are fine intercellular clefts (see fig. 74) which separate the cells from one another, but are bridged across by fibres which pass from cell to cell, and also through the substance of the cells (fig. 75) (Ranvier, Delépine). The intercellular channels serve for the passage of lymph, and within them lymph-corpuscles may occasionally be found, often having a stellate figure from becoming shaped to the interstices.

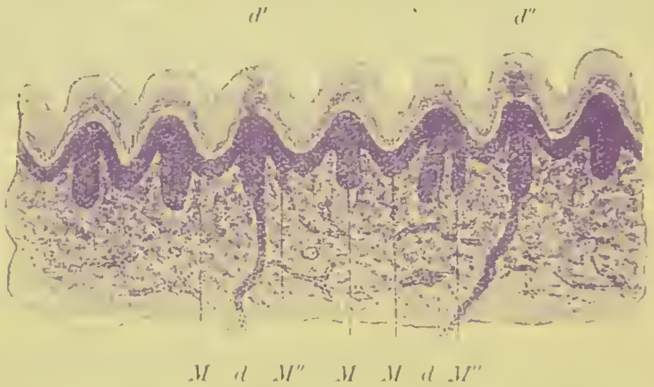

FIG. 330.—SECTION OF SKIN OF HEEL. (Blaschko.)

ep, epidermis; *c*, cutis vera; *d*, *d*, ducts of sweat-glands; *d'*, *d'*, their openings at the surface of the papillary ridge; *M*, Malpighian layer of epidermis thickened opposite the papillary ridges, where it dips down into the cutis vera (at *M'*, *M''*) leaving prominences of the cutis between.

The superficial layer of the rete mucosum is formed of somewhat flattened cells filled with granules or droplets of a material (*eleidin*) which stains deeply with carmine and hæmatoxylin (*stratum granulosum*, fig. 332; fig. 333). This is not sharply marked off from the cells of the rete mucosum which lie next to it, for many of these show similar granules, although they less completely fill the cell. Superficial to the stratum granulosum is a layer in which the cell-outlines are indistinct and the cells contain flakes or larger droplets of a hyaline material (*kerato-hyalin*), which stain less intensely than the granules in the last layer, and which tend to run together. This layer has a clear appearance in section, and is known as the *stratum lucidum.* Immediately superficial to the stratum lucidum is the *horny*

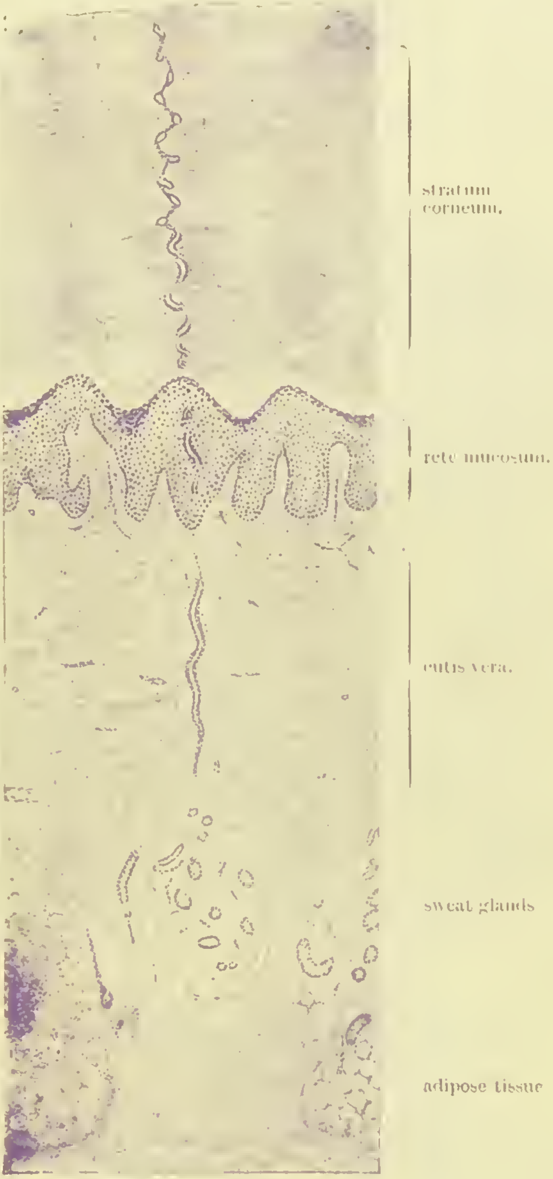

FIG. 331.—VERTICAL SECTION THROUGH THE SKIN OF THE SOLE OF THE FOOT. Magnified about 25 diameters.

part (*stratum corneum*) of the epidermis. It is composed of a number of layers of epithelium-cells, the nuclei of which are no longer visible. These cells near the surface take the form of thin horny scales which eventually become detached (fig. 334, *s*). In certain parts which have a thick epidermis and are not covered with hair (*e.g.* the palms and soles), the superficial part of the epidermis is a layer mainly formed by a number of greatly swollen cells (*sw*), forming collectively what has been termed the *epitrichial layer*. In the embryo in the second and third month of intrauterine life it covers the whole body, but is thrown off where hairs are developed.

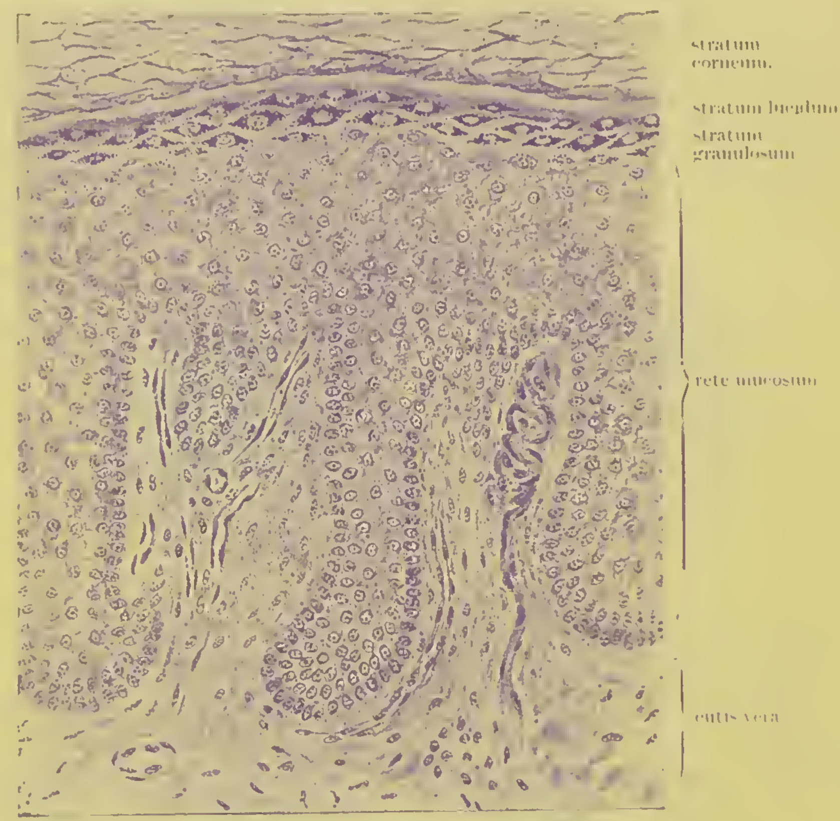

FIG. 332.—VERTICAL SECTION THROUGH THE SKIN OF THE PALMAR SIDE OF THE FINGER, SHOWING TWO OR THREE PAPILLÆ (ONE OF WHICH CONTAINS A TACTILE CORPUSCLE) AND THE DEEPER LAYERS OF THE EPIDERMIS. Magnified about 200 diameters.

The growth of the epidermis takes place by a multiplication of the cells of the deeper layers. The newly formed cells, as they grow, push towards the surface those which were previously formed, and in their progress the latter undergo a chemical transformation, which converts their fibrillated protoplasm into horny material: this change seems to occur just at and above the stratum granulosum (see fig. 332). The granules which occupy the cells of the stratum granulosum are

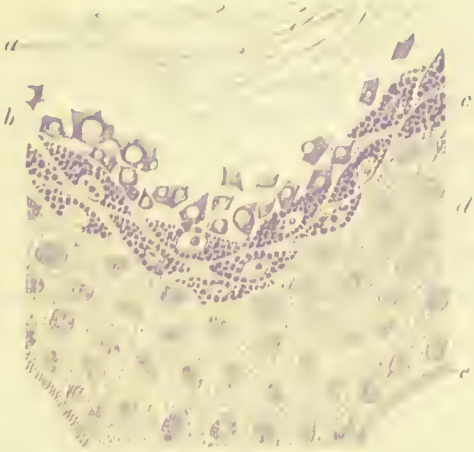

FIG. 333.—PORTION OF EPIDERMIS FROM A SECTION OF THE SKIN OF THE FINGER, COLOURED WITH PICROCARMINE. (Ranvier.)

a, stratum corneum; *b*, stratum lucidum with flakes of kerato-hyalin; *c*, stratum granulosum, the cells filled with drops of eleidin; *d*, prickle-cells; *e*, dentate projections by which the deepest cells of the epidermis are fixed to the cutis vera.

FIG. 334. SECTION OF EPIDERMIS (Ranvier.)

s, superficial horny scales; *sw*, swollen horny cells; *s.l.*, stratum lucidum; *p*, prickle-cells, several rows deep; *c*, elongated cells forming a single stratum near the corium; *s.gr*, stratum granulosum of Langerhans, just below the stratum lucidum. Part of a plexus of nerve-fibres is seen in the superficial layer of the cutis vera. From this plexus fine varicose nerve-fibrils may be traced passing up between the epithelium-cells of the Malpighian layer.

composed, as already stated, of a substance termed *eleidin*, which according to Ranvier becomes chemically altered and transformed into the *keratin* of the more superficial strata.

No blood-vessels pass into the epidermis, but it receives nerves which ramify between the cells of the rete mucosum in the form of fine varicose fibrils (fig. 334). In some parts these are enlarged at their extremity and along their course, into menisci which lie between the deeper epidermis cells. Such terminations are seen in the skin over the pig's snout (fig. 259) and in the root-sheaths of hairs. They also occur in the skin in the neighbourhood of the entrance of sweat-ducts into the epidermis (Ranvier) (fig. 335).

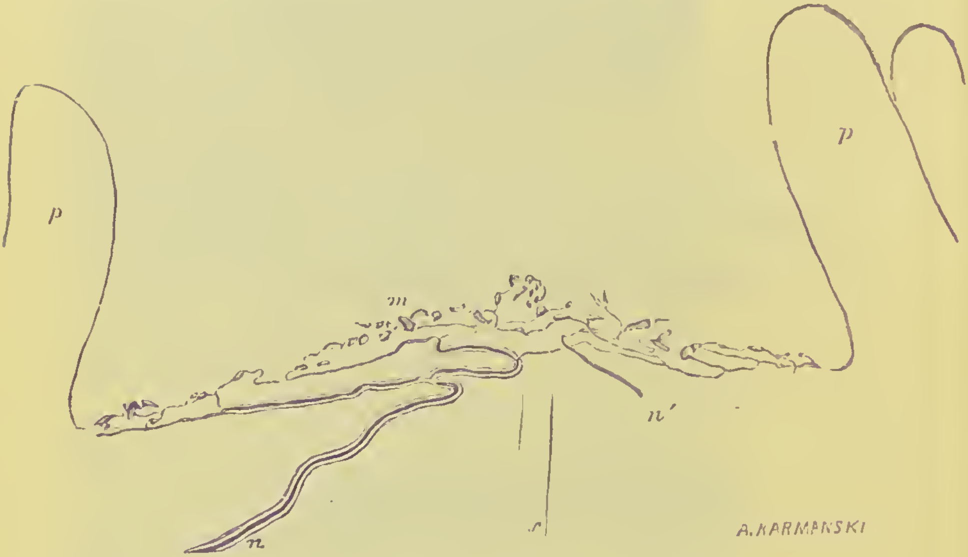

FIG. 335.—SECTION OF THE SKIN OF THE PULP OF THE FINGER OF A CHILD, STAINED WITH GOLD CHLORIDE, SHOWING NERVES TERMINATING IN AN IVY-LIKE ARBORESCENCE AT THE SURFACE OF THE CUTIS VERA AND IN THE DEEPEST PART OF THE EPIDERMIS. (Ranvier.)

p, *p*, outlines of papillæ; *n*, *n*′, nerve-fibres in cutis vera; *m*, terminal menisci; *s*, duct of a sweat-gland.

The **cutis vera** or corium is composed of dense connective tissue, which becomes more open and reticular in its texture in its deeper part, where it merges into the subcutaneous tissue. It is thickest over the posterior aspect of the trunk, whereas the epidermis is thickest on the palms of the hands and soles of the feet. The superficial or vascular layer of the corium bears microscopic *papillæ*, which project up into the epidermis, which is moulded over them. These papillæ for the most part contain looped capillary vessels, but some, especially those of the palmar surface of the hand and fingers, and the corresponding part of the foot, contain tactile corpuscles, to which medullated nerve-fibres pass (fig. 332).

In some parts of the body (scrotum, penis, nipple, and its areola), involuntary muscular tissue occurs in the deeper portions of the cutis vera, and, in addition, wherever hairs occur, small bundles of this tissue are attached to the hair-follicles.

The blood-vessels of the skin are distributed almost entirely to the surface, where they form a close capillary network, sending up loops into the papillæ (fig. 336). Special branches are also distributed to the various appendages of the skin, viz. the sweat-glands and hair-follicles, with their sebaceous glands and little muscles, as well as to the masses of adipose tissue which may be found in the deeper parts of the cutis.

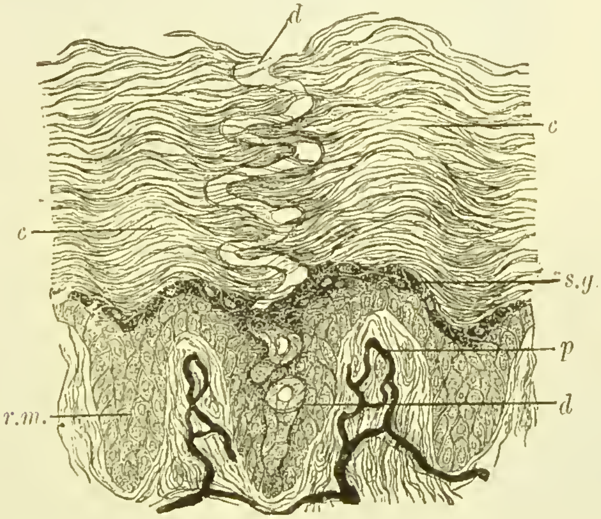

FIG. 336.—DUCT OF A SWEAT-GLAND PASSING THROUGH THE EPIDERMIS. Magnified 200 diameters. (Heitzmann.)

p, papillæ with blood-vessels injected; *r.m.*, rete mucosum between the papillæ; *c*, *c*, stratum corneum; *s.g.*, stratum granulosum; *d*, *d*, sweat-duct passing through epidermis.

The lymphatics originate near the surface in a network of vessels, which is placed a little deeper than the blood-capillary network. They receive branches from the papillæ, and pass into larger vessels, which are valved, and which run in the deeper or reticular part of the corium. From these the lymph is carried away by still larger vessels, which course in the subcutaneous tissue.

The **appendages of the skin** are the *nails*, the *hairs*, with their *sebaceous glands*, and the *sweat-glands*. They are all developed as thickenings and downgrowths of the Malpighian layer of the epidermis.

The Nails.

The **nails** are thickenings of the deeper part of the stratum corneum developed over a specially modified portion of the skin (fig. 337), which is known as the *bed of the nail*, the depression at the posterior part of the nail-bed from which the root of the nail grows being known as the *nail-groove*. The part of the bed which occupies the inner or central portion of the groove is termed the *nail-matrix*, since it is from this part that the growth of the nail proceeds. The distal part of the nail forms the *free border*, and is the thickest part of the body of the nail. The substance of the nail is composed of clear horny cells, somewhat like the cells of the stratum lucidum of the rest of the epidermis. Each contains the remains of a nucleus. The nail proper rests immediately upon a Malpighian layer similar to that which is found in the epidermis generally, but destitute of a defined stratum granulosum. Nevertheless, in the more superficial cells both of the bed and matrix there are a large number of granules to be seen, which appear to

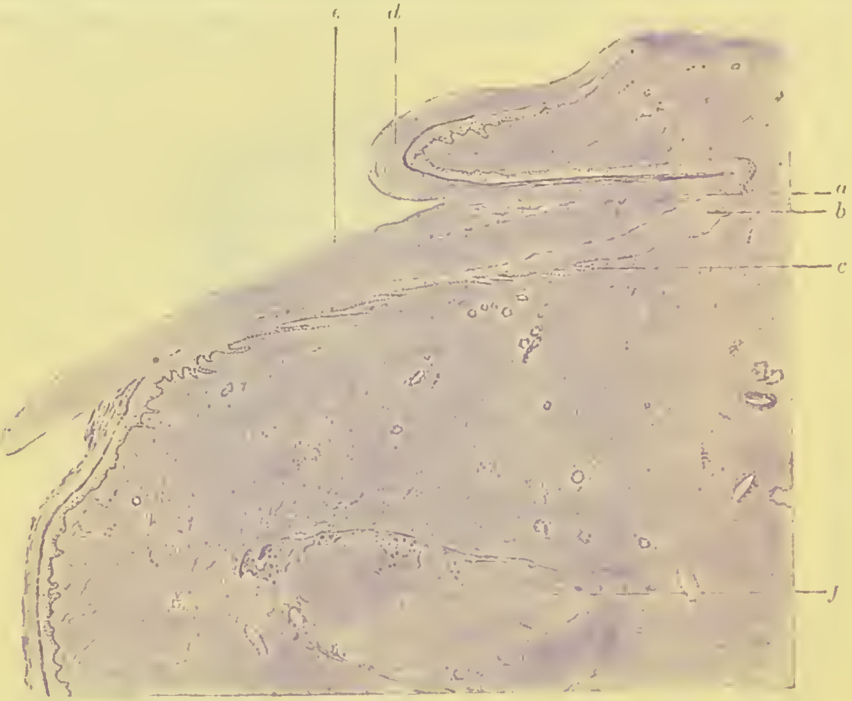

Fig. 337.—Longitudinal section through the root of the nail and its matrix. Magnified about 10 diameters.

a, root of nail; *b*, Malpighian layer of matrix: *c*, ridges in dermis of nail-bed; *d*, epitrichial layer of epidermis; *e*, eponychium; *f*, bone (terminal phalanx) of finger.

represent those of the stratum granulosum of the epidermis. These granules are, however, not composed of eleidin, but of a material (*onychogenic substance*, Ranvier) which stains brown instead of red with carmine; a similar material occurs in the cells which form the fibrous substance and cuticula of the hairs. The corium of the nail-bed is beset with longitudinal ridges instead of the papillæ which are

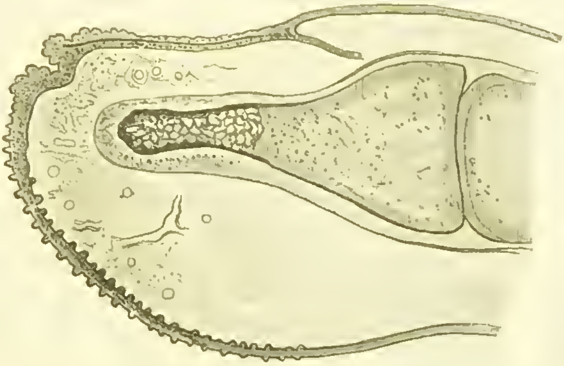

FIG. 338.—SECTION THROUGH END OF FINGER OF HUMAN EMBRYO AT THE TIME OF THE COMMENCEMENT OF FORMATION OF THE NAIL. (Kölliker.)

Notice the ossification of the terminal phalanx beginning at the tip of the cartilage. In the thickened epidermis over this the commencing nail is seen as a dark line.

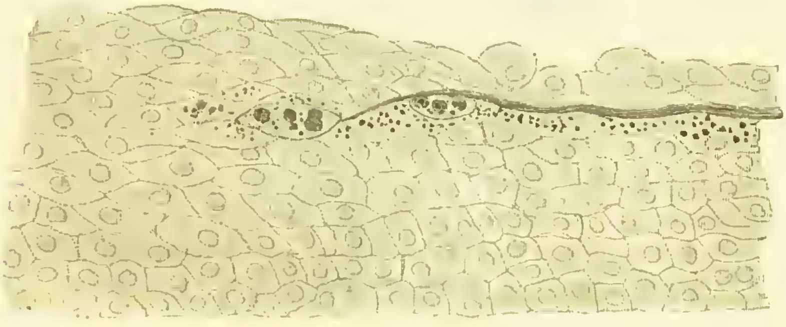

FIG. 339.—FIRST APPEARANCE OF NAIL SUBSTANCE IN THE FORM OF GRANULES OF ONYCHOGENIC MATERIAL IN SOME OF THE CELLS COVERING THE NAIL-BED. (Kölliker.)

present over the rest of the skin; these, like the rest of the superficial part of the corium, are extremely vascular.

The nail-bed also receives many nerve-fibres. Some of these end in Pacinian corpuscles, whilst others ramify in the ridges of the corium, and others again penetrate amongst the deeper epithelium cells.

The nails are developed in the fœtus at about the third month (fig. 338), the groove being formed at this time in the corium, and the nail rudiment appearing in it as a development of onychogenic substance in some of the cells of the epithelium, which lies over the bed (fig. 339). It becomes free in the sixth month, its free end being at first thin, but as it grows forward over the bed it receives additions on its under surface—at least in the posterior part of the bed—so that after a time the distal end becomes thicker. The epitrichial layer of the cuticle which originally covered the developing nail becomes detached after the fifth month, and, after birth, only remains as the narrow border of cuticle (*eponychium*) which overlies the *lanula* at the root.

Hairs.

The **hairs** are growths of the epidermis, developed in little pits—the *hair-follicles*—which extend downwards into the deeper part of the corium, or even into the subcutaneous tissue. The hair grows from the bottom of the follicle, the part which thus lies within the follicle being known as the *root.*

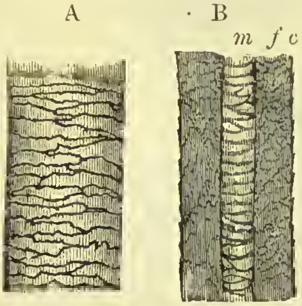

Fig. 340.—Piece of human hair. Magnified.

A, seen from the surface; B, in optical section. *c*, cuticle; *f*, fibrous substance; *m*, medulla, the air having been expelled by Canada balsam.

The substance of a hair is mainly composed of a pigmented, horny, *fibrous material* (fig. 340, *f*), which can be separated by the action of sulphuric acid into long tapering fibrillated cells, the nuclei of which are still visible. The fibrous substance of the hair is covered by a layer of delicate imbricated scales, termed the *hair-cuticle* (*c*). In many hairs, but not in all, the centre is occupied by an axial substance (*medulla*, *m*), formed of angular cells which contain granules of eleidin, and frequently have a dark appearance from the presence of minute air-bubbles. The latter may also occur in interstices in the fibrous substance. When they are present, the hair looks white by reflected light. The *root* has the same structure as the body of the hair, except at its extremity, which is enlarged; this enlargement is composed mainly of soft, growing cells, and fits over a vascular *papilla*, which projects up into the bottom of the follicle (fig. 341).

Structure of hair-follicle (figs. 341 to 344).—The follicle, like the skin itself, of which it is a recess, is composed of two parts: one epithelial, and the other connective-tissue. The epithelial or epidermic part of the follicle closely invests the hair-root, and is often in great part dragged out with it; hence it is known as the *root-sheath.* It consists of an outer layer of soft columnar and polyhedral cells, like the

Malpighian layer of the epidermis, but without stratum granulosum—the *outer root-sheath*; and of an inner, thinner, horny stratum next to the hair—the *inner root-sheath.* The inner root-sheath itself consists of three layers, the outermost being composed of horny, fibrous, oblong cells the nuclei of which are obscure and difficult to make out (*Henle's layer*), the next of polyhedral nucleated cells containing eleidin (*Huxley's layer*), and the third—the *cuticle of the root-sheath*—a layer of downwardly imbricated scales, which fit over the upwardly imbricated scales of the hair itself. In the more superficial part of the hair follicle the layers of Huxley and Henle are indistinguishable, the cells of both being clear and keratinised; even lower down where distinguishable they show a tendency to dovetail into one another. At the bottom of the follicle no differentiation into layers can be made out in the root-sheath, which is here formed by a uniform mass of soft cells surrounding the papilla.

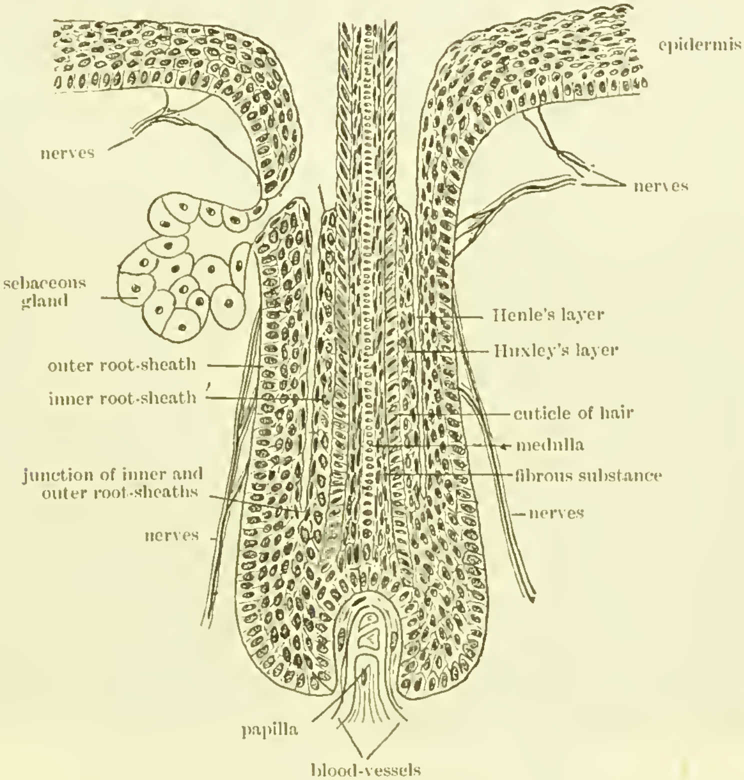

FIG. 341.—DIAGRAM TO EXPLAIN THE FORMATION OF A HAIR. (Maurer.)

In the greater extent of the follicle the outer root-sheath is several layers deep, but as the bottom of the follicle is approached it becomes thinner, and is finally reduced to a single stratum of cells which becomes flattened out into a very thin layer in the papillary part (fig. 342, I.).

The connective tissue or dermic part of the hair-follicle is composed internally of a vascular layer, which is separated from the root-sheath by a basement-membrane termed the *hyaline layer* of the follicle. This inner vascular layer corresponds to the superficial layer of the cutis vera. Its fibres and cells have a regular circular arrangement around the follicle, the cells being flattened against the hyaline layer. Externally the dermic coat of the follicle has a more open texture, corresponding to the deeper part of the cutis, and contains the larger

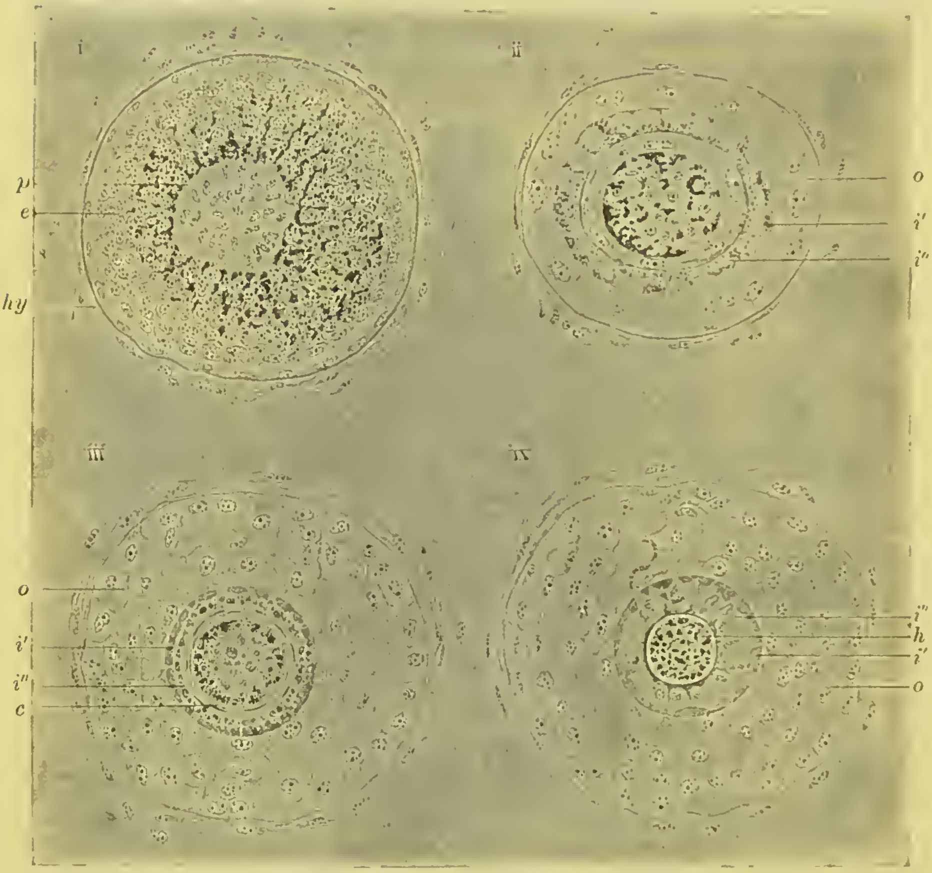

FIG. 342.—SECTIONS ACROSS HAIR-FOLLICLES FROM THE SCALP OF AN INFANT.

I. Through papilla. II. Just above papilla. III. About middle of follicle. IV. Near outer part of follicle. In I.:—*p*, papilla; *e*, epithelium surrounding papilla, with pigment in cells; *hy*, hyaline layer of dermic coat with thin outer root-sheath just within it. In II., III., IV.:—*o*, outer root-sheath; *i'*, layer of Henle and *i''*, layer of Huxley of the inner root-sheath; *c*, cuticle of root-sheath; *h*, hair.

branches of the arteries and veins. In the large tactile hairs of animals, the veins near the bottom of the follicle are dilated into sinuses, so as to produce a kind of erectile structure.

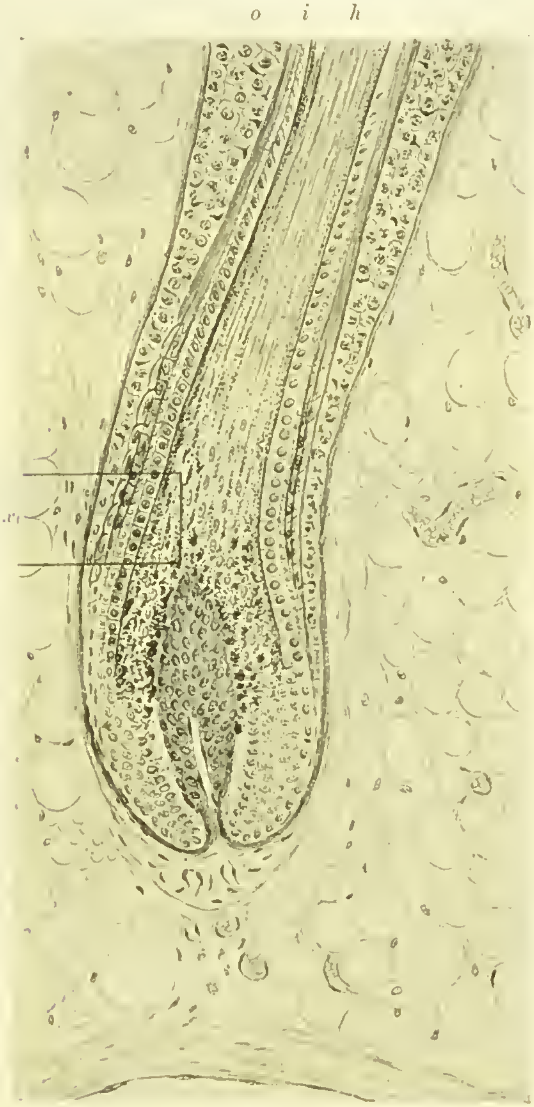

Fig. 343.—Longitudinal section of a hair-follicle. Magnified 200 diameters. *o*, outer; *i*, inner root-sheath; *h*, hair; *x*, part shown magnified in fig. 344.

The hair-follicle receives nerve-fibres which pass into the papilla, and others which enter the root-sheath. These last are derived from the superficial nerves of the corium and form ring-like arborisations in the upper part of the hair-follicle. They are especially well

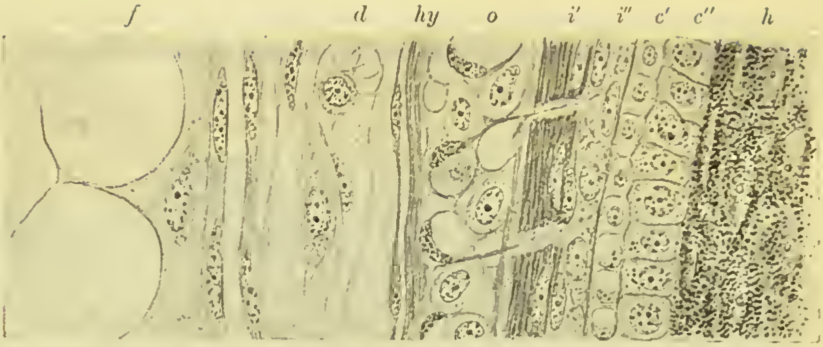

FIG. 344.—A SMALL PORTION OF THE SECTION SHOWN IN FIG. 343 ENLARGED TO EXHIBIT THE STRUCTURE OF THE SEVERAL LAYERS.

h, hair ; *c''*, its cuticle ; *c'*, cuticle of root-sheath ; *i''*, Huxley's layer ; *i'*, Henle's layer ; *o*, outer root-sheath ; *hy*, hyaline layer ; *d*, dermic coat ; *f*, fat-cells.

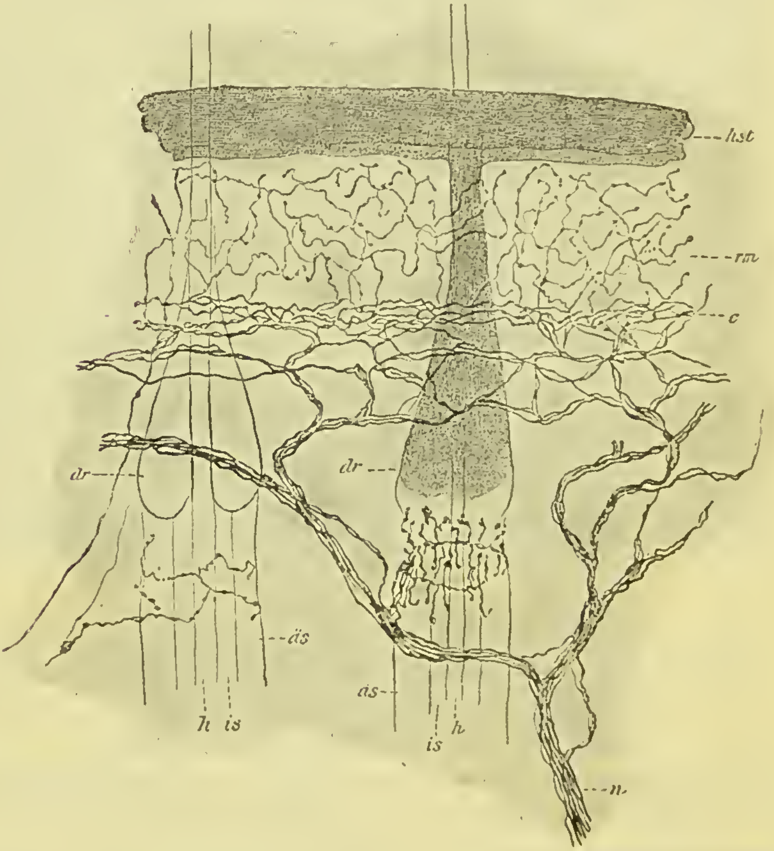

FIG. 345.—NERVES AND NERVE-ENDINGS IN THE SKIN AND HAIR-FOLLICLES. (G. Retzius.)

h,t, horny stratum ; *rm*, rete Malpighii ; *c*, superficial nerve-fibre plexus in the cutis ; *n*, cutaneous nerve ; *is*, inner root-sheath of hair ; *äs*, outer root-sheath ; *h*, hair ; *dr*, sebaceous glands.

developed in the large tactile hairs (whiskers) of animals (figs. 345, 347).

The hair grows from the bottom of the follicle by multiplication of the soft cells which cover the papilla, these cells becoming elongated and pigmented to form the fibres of the fibrous substance, and otherwise modified to produce the medulla and cuticle of the hair and the several layers of the root-sheath. The cells which form the medulla of the hair and the inner root-sheath are filled with granules of eleidin, but those which form the fibrous substance and cuticula of the hair have granules which stain brown with carmine, and appear similar to those which are met with in the corresponding cells of the nail-matrix (Ranvier) (see p. 267).

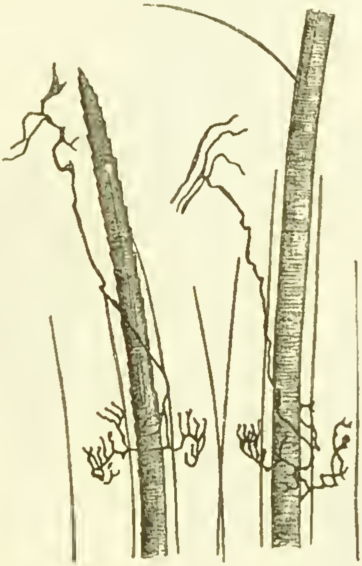

FIG. 346.—FROM A SECTION OF SKIN PREPARED BY THE CHROMATE OF SILVER METHOD, SHOWING THE UPPER PART OF TWO HAIRS AND THE TERMINAL ARBORISATIONS OF NERVE-FIBRES IN THEIR ROOT-SHEATHS. (Van Gehuchten.)

On the side to which the hair slopes a small patch of richly innervated thickened epidermis is usually to be found, developed over an enlarged papilla of the cutis vera: while on the opposite side of the hair is a flat area of skin with thickened scale-like epidermis, which may represent a vestige of the reptilian scale (Pinkus).

The hair-germs when they first appear (as at *a*, fig. 349) are singularly like certain tactile patches which are found in the skin of amphibia and some reptiles, and it is possible that hairs have become developed phylogenetically from these patches. It is well known that the tactile sensibility of many parts of the skin is intimately associated with the hairs, where these occur, although parts devoid of hairs may also have a highly developed sense of touch.

Besides the hair-follicles already described, which are provided with a papilla, from the cells on the surface of which the hair and its inner root-sheath grow (*growing hairs, papillated hairs, hairs with hollow bulb*), there are many hairs which are unprovided with a papilla and the follicle of which ceases at the level of attachment of the arrector pili muscle (*club hairs, non-papillated hairs, hairs with solid bulb*). These are hairs which have lost their papilla and have ceased to grow; they are more easily eradicated than the growing hairs, and tend to fall out spontaneously after a time. In their follicles the whole of the lower part, including the original papilla and the soft growing cells which cover it, have entirely disappeared, the hair being now attached at its sides and below to the root-sheath. A hair which has thus ceased to grow eventually becomes lost, but its place is presently supplied by a new hair, which becomes developed in a down-growth from the bottom of the follicle, a new papilla becoming formed at the extremity of the down-growth (fig. 348). If not previously detached, the old hair is pushed out from the follicle by the one which replaces it.

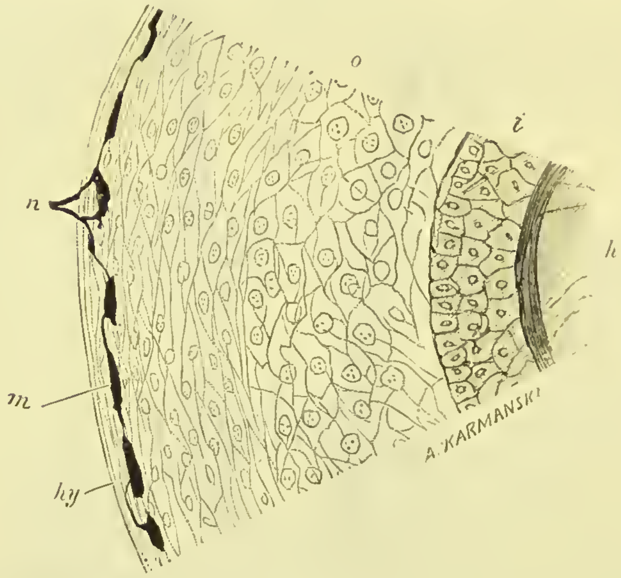

FIG. 347.—NERVE ENDING IN OUTER ROOT-SHEATH OF TACTILE HAIR OF RABBIT. (Ranvier.)

n, nerve-fibre; *m*, tactile meniscus; *o*, outer root-sheath; *i*, inner root-sheath; *h*, hair; *hy*, hyaline membrane.

The detachment of the non-papillated hairs is preceded by an absorption of the root of the hair and of the investing inner root-sheath. This absorption appears to be effected by the cells of the outer sheath, which multiply at the expense of the keratinised parts of the hair root and thus undermine its attachment to the follicle (fig. 348).

The hairs are originally developed in the embryo in the form of small solid down-growths from the Malpighian layer of the epidermis

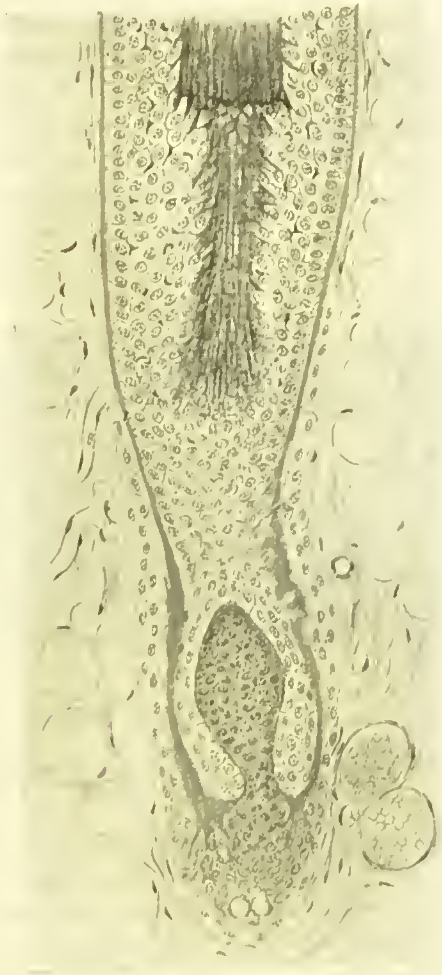

FIG. 348.—LONGITUDINAL SECTION THROUGH THE FOLLICLE OF A HAIR WHICH HAS CEASED TO GROW AND THE ROOT OF WHICH IS UNDERGOING ABSORPTION. Magnified 200 diameters.

(fig. 349). The hair-germ, as it is called (although it gives rise not only to the hair proper but also to the epithelium-cells of the hair-follicle), is at first composed entirely of soft growing cells, the outermost and deepest having a columnar shape; but presently those in the centre become differentiated, so as to produce a minute hair invested by inner root-sheath, its base resting upon a papilla which has become inclosed by the extremity of the hair-germ and which is continuous with the connective tissue of the corium (figs. 350, 351). As the minute hair grows, it pushes its way through the layers of the epidermis, which it finally perforates, the epitrichial layer being thrown off (p. 262). At the same time the follicle grows more deeply into the cutis vera, carrying the papilla down with it.

The hair-rudiments begin to appear at the third or fourth month of fœtal life; their growth is completed about the fifth or sixth month, and the fine hairs which they form constitute a complete hairy covering termed the *lanugo*. This is entirely shed within a few months of birth, the new hairs being formed in down-growths from the old hair-follicles in the manner already mentioned.

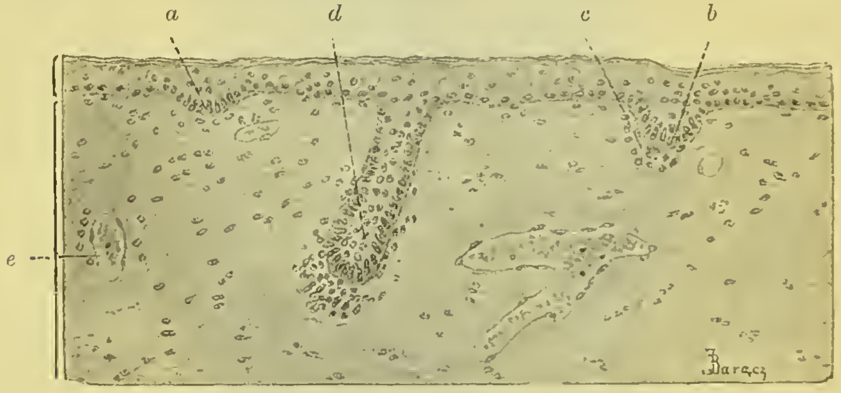

FIG. 349.—HAIR-GERMS IN A SECTION OF THE SCALP OF A HUMAN FŒTUS. (Szymonowicz.) Magnified 230 diameters.

a, commencing down-growth of epidermis; *b*, further stage of down-growth; *c*, connective-tissue cells beginning to accumulate to produce the dermic coat of the follicle; *d*, hair-follicle more advanced in development; *e*, section of a blood-vessel.

Hairs grow at the rate of half an inch per month. They are found all over the surface of the body except on the palms of the hands and the soles of the feet, and on the distal phalanges of the fingers and toes. They usually slant, and in the negro the hair-follicles are even considerably curved. On the scalp they are set in groups, as is well seen in a horizontal section.

The hairs of animals are often curiously marked by the arrangement of their medulla, the markings being characteristic of particular species. In some animals, *e.g.* the mole, the hairs have a varicose form with alternate enlargements and constrictions. In human hair the disappearance of the papilla is preceded by its gradual diminution in size, and during this period the root of the hair is becoming gradually more slender (Ranvier), so that when such a hair is pulled out it appears to be of least diameter near the bulb, instead of being largest there, as is the case under ordinary circumstances.

Muscles of the hairs.—A small muscle composed of bundles of plain muscular tissue is attached to each hair-follicle (*arrector pili*); it passes from the superficial part of the corium, on the side to which the hair slopes, obliquely downwards, to be attached near the bottom of the follicle to a projection formed by a localised hypertrophy of the outer root-sheath. When the muscle contracts, the hair becomes more erect, and the follicle is dragged upwards so as to cause a prominence on the general surface of the skin, whilst the part of the corium from which the little muscle arises is correspondingly depressed; the roughened condition known as 'goose skin' being in this way produced. There is always a sebaceous gland in the triangle formed between the arrector pili, the mouth of the hair-follicle, and the epidermis, so that the contraction of the arrector generally causes the secretion of the gland to be extruded.

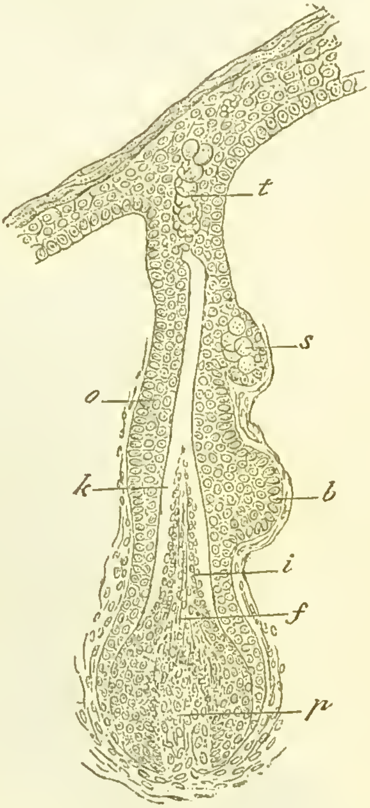

FIG. 350.—DEVELOPING HAIR FROM HUMAN EMBRYO OF 4½ MONTHS. (Ranvier.)

p, papilla; *f*, hair-rudiment; *i*, cells from which the inner root-sheath is becoming formed; *k*, keratinised part of inner root-sheath, uncoloured by carmine; *o*, outer root-sheath; *b*, epithelial projection for insertion of arrector pili; *s*, sebaceous gland; *t*, sebaceous degeneration of cells in the part which will become the neck of the follicle. This forms a channel for the passage of the hair-point through the Malpighian layer.

GLANDS OF THE SKIN.

The **sebaceous glands** (fig. 341) are small saccular glands, the ducts from which open into the mouths of the hair-follicles, but they are also found in a few situations which are devoid of hairs (margin of lips, labia minora, glans, and prepuce). The Meibomian glands of the eyelid may also be regarded as modified sebaceous glands. Both the duct and the saccules are lined by epithelium, which becomes charged with fatty matter. This sebaceous matter is discharged into the cavity of the saccule, probably owing to the disintegration of the cells within which it is formed. There may be more than one sebaceous gland attached to each hair-follicle.

The sebaceous glands are developed as outgrowths from the outer root-sheaths (figs. 350, 351, *s*).

The **sweat-glands** are abundant over the whole skin, but they are most numerous on the palm of the hand and on the sole of the foot. They are composed of coiled tubes, which lie in the deeper part of the integument and send their ducts up through the cutis to open on the surface by corkscrew-like channels in the epidermis (figs. 330, 331, 336).

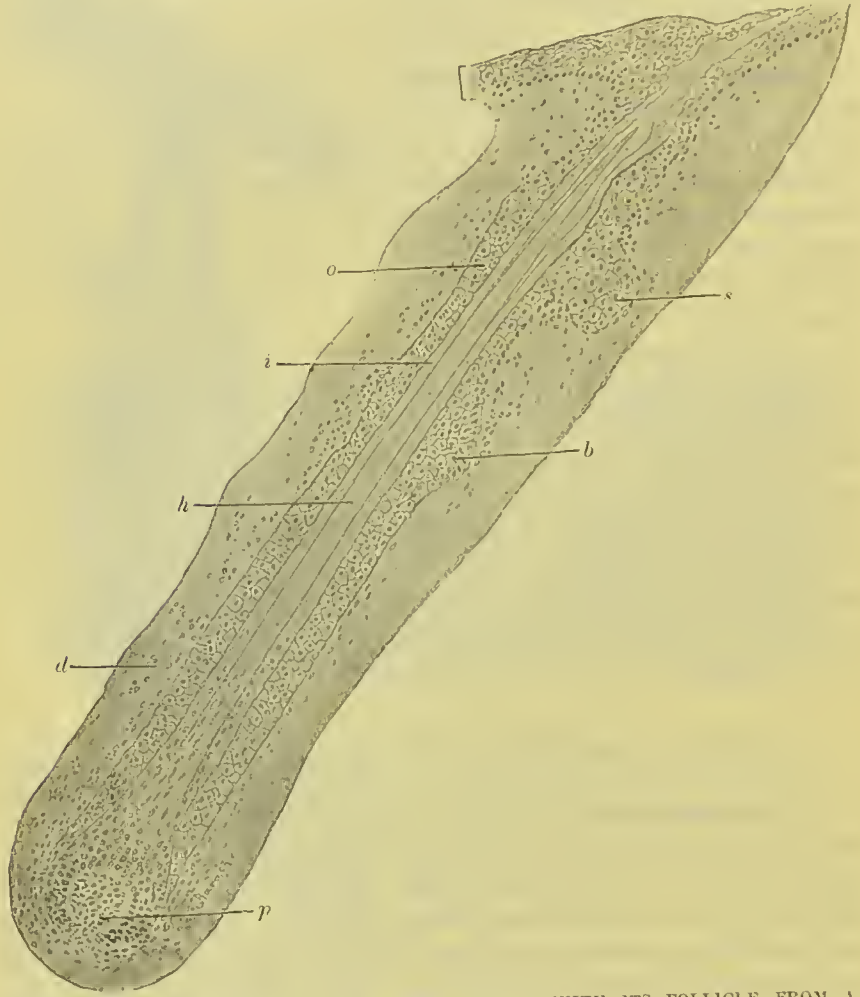

FIG. 351.—LONGITUDINAL SECTION OF A HAIR WITH ITS FOLLICLE FROM A SIX-MONTHS' HUMAN EMBRYO. (Szymonowicz.) Magnified about 150 diameters.

p, papilla; *h*, young hair; *i*, inner root-sheath; *d'*, dermic coat of follicle; *o*, outer-root-sheath; *s*, sebaceous gland rudiment; *b*, projection for insertion of arrector pili.

The *glandular* or *secreting tube* is a convoluted tube composed of a basement-membrane lined by a single layer of cubical or columnar epithelium-cells, and with a layer of longitudinally or obliquely disposed fibres between the epithelium and basement-membrane (fig. 352). These fibres are usually regarded as muscular, but the evidence on this point is not conclusive. The secreting tube is considerably larger than the *efferent tube* or *duct*, which begins within the gland and usually makes several convolutions before leaving the gland to traverse the cutis vera. The efferent tube has an epithelium consisting of two or three layers of cells, within which is a well-marked cuticular lining, but there is no muscular layer. The passage through the epidermis has no proper wall, but is merely a channel excavated between the epithelium-cells. Very large sweat-glands occur in the axilla.

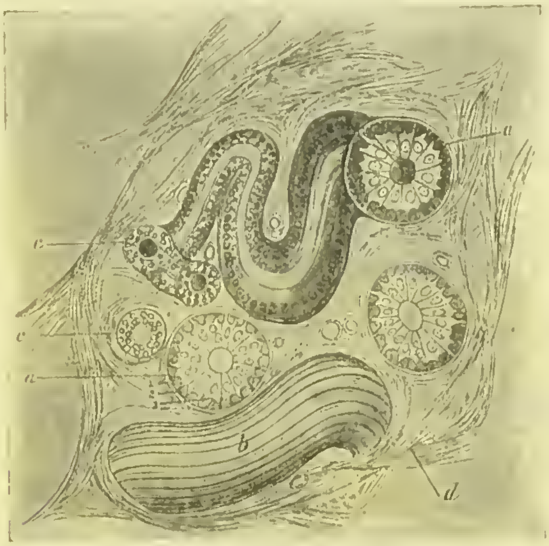

FIG. 352.—SECTION OF A SWEAT-GLAND IN THE SKIN OF MAN.

a, *a*, secreting tube in section; *b*, a coil seen from above; *c*, *c*, efferent tube; *d*, intertubular connective tissue with blood-vessels. 1, basement-membrane; 2, muscular fibres cut across; 3, secreting epithelium of tubule.

The *ceruminous glands* of the ear (fig. 353) are modified sweat-glands. The secretion is of a sebaceous nature, instead of being watery like that of the ordinary sweat-glands. They are closely associated with large sebaceous glands (fig. 354).

The sweat-glands are developed, like the hairs, from down-growths of the Malpighian layer of the epidermis into the corium. They are distinguishable from the hair-germs by the fact that the cells of the outermost layer are not columnar in shape, but spheroidal or polyhedral. The sweat-gland germs which are thus formed become eventually coiled up at their extremities and converted into hollow tubes. The muscular fibres of the tubes as well as the secreting epithelium-cells are ectodermic structures.

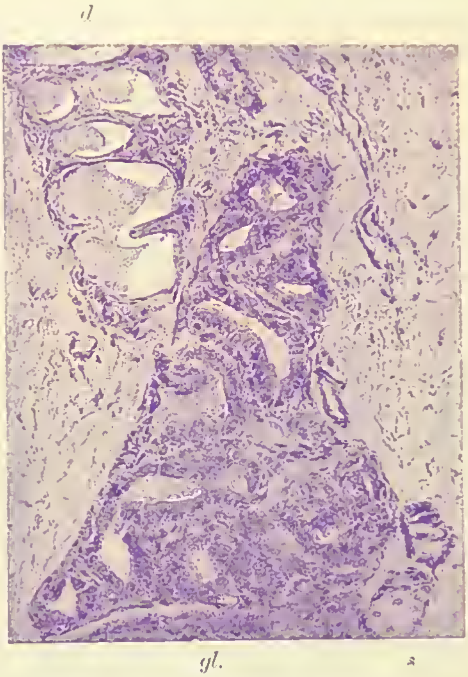

FIG. 353.—SECTION OF CERUMINOUS GLAND OF THE EXTERNAL EAR. Photograph.

d, duct of gland, having a spiral course and therefore cut several times; it is partly filled with cerumen; *gl*, secreting tubules of gland; *s*, extremity of a tubule of a sebaceous gland which extended as far as the base of the ceruminous gland.

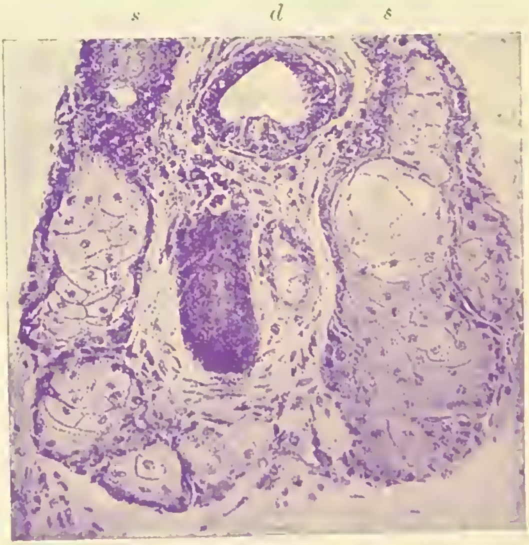

FIG. 354.—SECTION SHOWING THE DUCT OF A CERUMINOUS GLAND ACCOMPANIED BY THE SECRETING TUBULES OF LARGE SEBACEOUS GLANDS. Photograph.

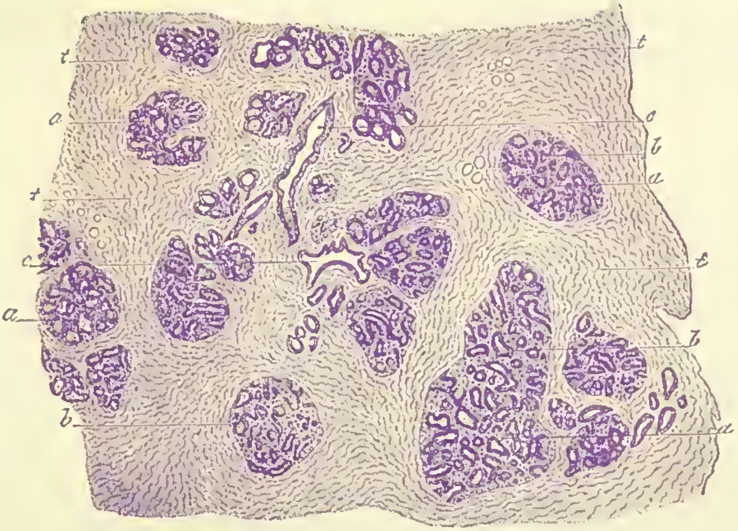

FIG. 355.—SECTION OF MAMMARY GLAND OF WOMAN DURING LACTATION. (Testut, after de Sinéty.)

a, lobule of gland; *b*, acini lined by cubical epithelium; *c*, duct; *t*, connective-tissue stroma.

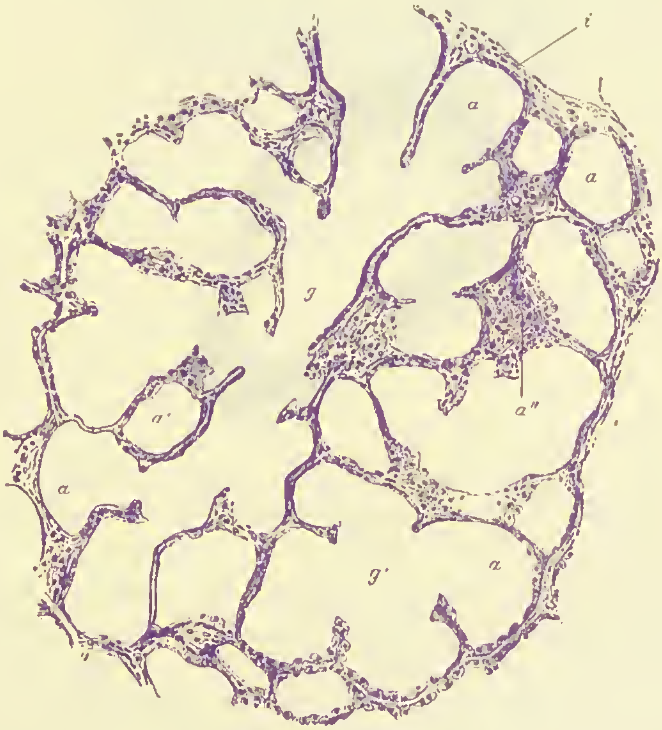

FIG. 356.—SECTION OF MAMMARY GLAND, HUMAN, IN FULL ACTIVITY. (v. Ebner.) × 110.

a, *a'*, *a''*, alveoli variously cut, and distended by secretion; *g*, *g'*, commencing ducts; *i*, connective tissue.

The sweat-glands receive nerve-fibres, and each gland has a special cluster of capillary blood-vessels.

THE MAMMARY GLANDS.

The **mammary glands** are compound racemose glands which open by numerous ducts upon the apex of the nipple. The ducts are dilated into small reservoirs just before reaching the nipple. If traced backwards, they are found to commence in groups of saccular alveoli (fig. 355). The walls of the ducts and alveoli are formed of a basement-membrane lined by a simple layer of flattened epithelium (fig. 356). Milk globules may be seen within the alveoli and ducts, and at the commencement of lactation amœboid cells containing fat particles appear in the secretion (*colostrum corpuscles*). These are probably emigrated leucocytes similar to the salivary corpuscles of saliva, but some authors have looked upon them as epithelium-cells or portions of epithelium-cells which have become detached from the general lining of the alveoli.

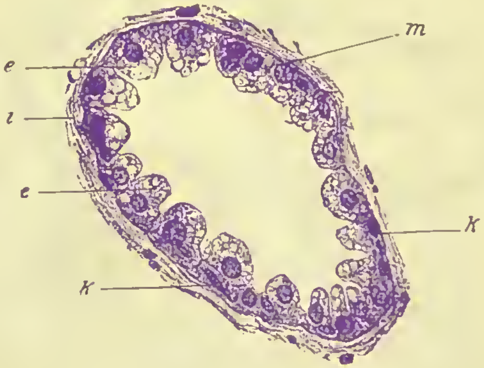

FIG. 357.—AN ALVEOLUS WITH FAT-DROPS IN CELLS. (v. Ebner.) × 360.
e, cells of alveolus; *k*, cells forming basket-like basement-membrane, *m*; *i*, connective tissue.

Development.—The mammary glands are developed in the same manner as the sweat-glands, excepting that the secreting part does not become convoluted and tubular. In the virgin mamma they show very few and small groups of alveoli, but as pregnancy advances the gland ducts bud out extensively, and many more alveoli are formed and undergo enlargement, until the greater part of the connective tissue in the mammary region is permeated by them. In sections of the gland they may be seen in various stages of development (figs. 356, 358). After lactation is over they undergo a process of retrogression.

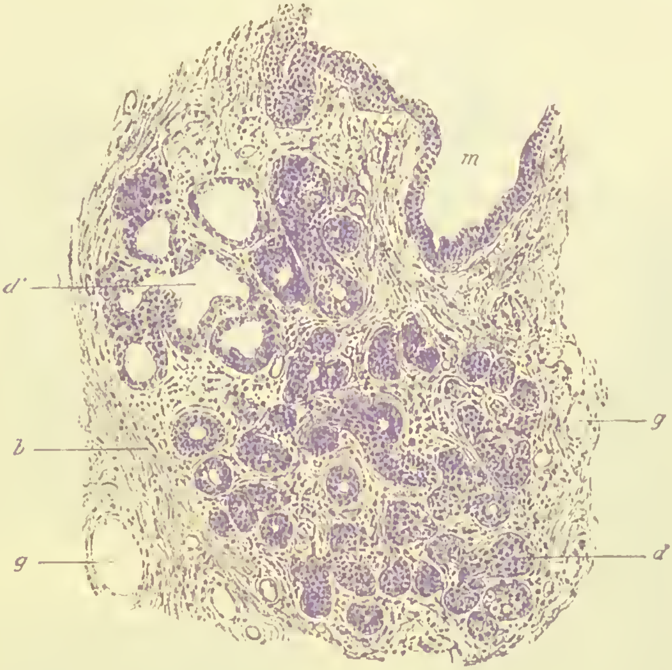

FIG. 358.—SECTION FROM THE SAME GLAND AS THAT SHOWN IN FIG. 355. (v. Ebner.) ×110.

b, connective tissue; *d*, undeveloped alveoli; *d'*, partially developed alveoli; *g*, blood-vessels; *m*, portion of larger duct with two-layered epithelium.

LESSON XXVI.

STRUCTURE OF THE HEART.

1. In sections through the wall of the auricle note the relative thickness of the epicardium, myocardium, and endocardium. Observe the blood-vessels and nerve fibres under the epicardium, often embedded in fat; here and there a ganglion may be seen under this membrane. Notice also the elastic networks under both the pericardium and endocardium. Make a general sketch from this section.

2. In sections through the wall of the ventricle the same points are to be noticed. The muscular fibres are variously cut. In those which are cut longitudinally, the branching of the fibres and their union both laterally and by their branches may be seen. Notice also that although the fibres are cross-striated this is less distinct than in voluntary muscle, and that the nuclei lie near the centre of each fibre. Transverse markings may also be seen passing across the fibres between the nuclei; this is usually taken as indicating a division into cells. The endocardium is very thin, especially over the columnæ carneæ.

3. Section through one of the valves of the heart.[1]

4. If a portion of endocardium of the sheep's heart is spread out on a slide and examined in salt solution, a network of large beaded fibres may be seen with a low power or even with a lens; they are also well seen in sections. These are the fibres of Purkinje; they are formed of large, square-looking cells usually containing two nuclei, and having striated muscular substance at their periphery. The fibres of Purkinje may also be seen in sections.

5. The lymphatics of the heart may be injected with Berlin blue by sticking the nozzle of the injecting syringe into the muscular substance, in the interstices of which the lymphatics arise. These commencing lymphatics lead to efferent vessels which pass under the epicardium towards the base of the heart.

6. The epithelium which covers the epicardium, and that which lines the endocardium, may be studied in preparations of the fresh organ which have been well rinsed with distilled water; then treated with nitrate of silver, again rinsed, and subsequently exposed to the light and hardened in alcohol. Surface sections are to be made and mounted in xylol balsam or dammar.

The muscular tissue of the heart (*myocardium*) forms the main thickness of the ventricles and also of parts of the auricles. It is composed of a network of fibres which are formed of uninucleated transversely striated cells, the structure of which has already been studied (Lesson XVII.).

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[1] The appearances which are to be studied in sections 1, 2, and 3 can all be obtained in one preparation, viz. a vertical section including a portion of auricle and ventricle and a flap of the intervening auriculo-ventricular valve.

In the interstices of the muscular bundles there is a little areolar tissue in which run the very numerous blood-capillaries and the lacunar lymphatics.

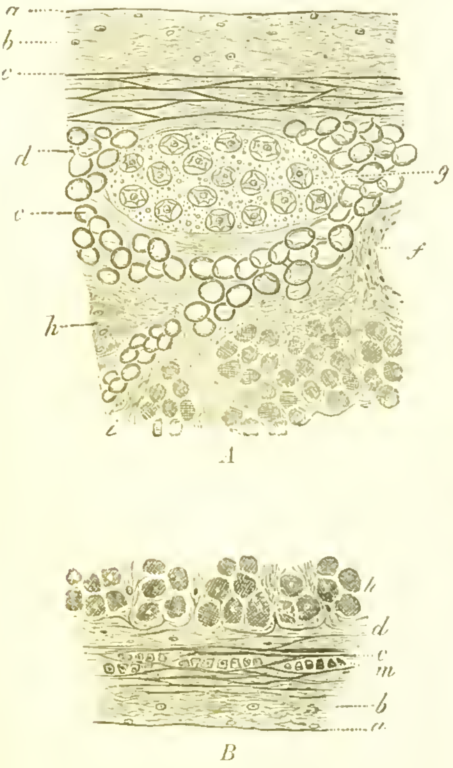

Fig. 359 A, B.

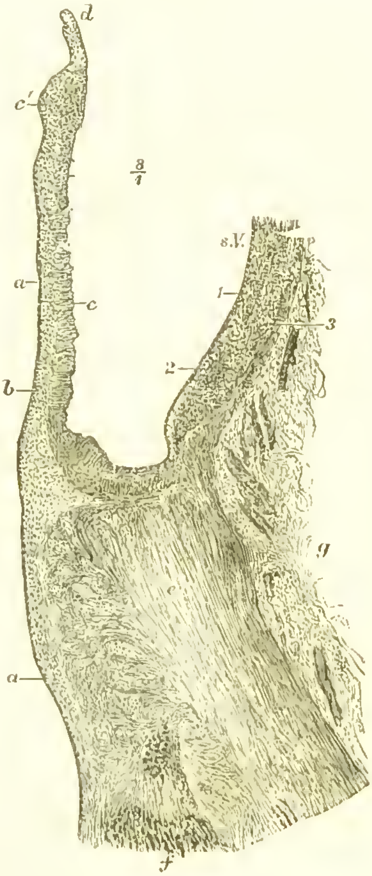

Fig. 360.

Fig. 359 A, B.—Sections of the right auricle.

A, Epicardium and adjacent part of the myocardium. *a*, serous epithelium in section; *b*, connective tissue layer; *c*, elastic network; *d*, subserous areolar tissue; *e*, fat; *f*, section of a blood-vessel; *g*, a small ganglion; *h*, muscular fibres of the myocardium; *i*, intermuscular areolar tissue.

B, Endocardium and adjacent layer of the myocardium. *a*, lining epithelium; *b*, connective tissue with fine elastic fibres; *c*, layer with coarser elastic fibres; *d*, subendocardial connective tissue continuous with the intermuscular tissue of the myocardium; *h*, muscular fibres of the myocardium; *m*, plain muscular tissue in the endocardium.

Fig. 360.—Section through one of the flaps of the aortic valve, and part of the corresponding sinus of Valsalva, with the adjoining part of the ventricular wall. (Horsley.)

a, endocardium, prolonged over the valve; *b*, sub-endocardial tissue; *c*, fibrous tissue of the valve, thickened at *c′* near the free edge; *d*, section of the lunula; *e*, section of the fibrous ring; *f*, muscular fibres of the ventricle attached to it; *g*, loose areolar tissue at the base of the ventricle; *s.V.*, sinus of Valsalva; 1, 2, 3, inner, middle, and outer coats of the aorta.

The myocardium is covered externally by a layer of serous membrane—the *epicardium* (cardiac pericardium, fig. 359, *A*)—composed like other serous membranes, of connective tissue and elastic fibres,

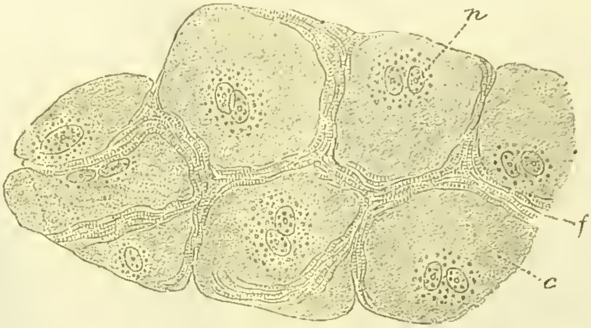

FIG. 361.—FRAGMENT OF THE NETWORK OF PURKINJE'S FIBRES FROM THE VENTRICULAR ENDOCARDIUM OF THE SHEEP. (Ranvier.)

c, clear cell body ; *n*, nuclei ; *f*, striated fibrils.

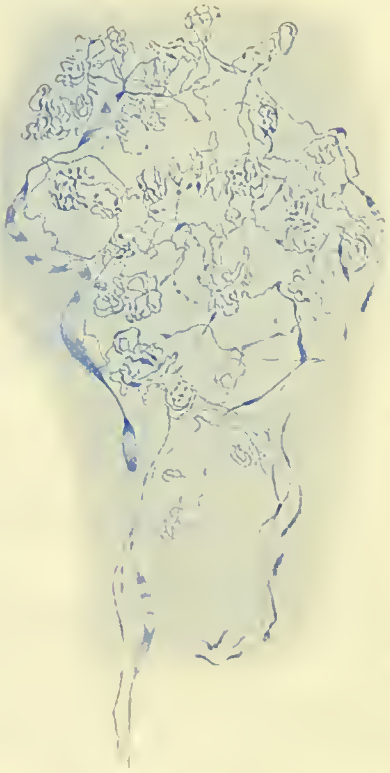

FIG. 362.—ENDING OF MEDULLATED NERVE-FIBRES, PROBABLY DERIVED FROM THE VAGUS, IN A SMALL CARDIAC GANGLION. (Dogiel.)

The ganglion cells are not represented.

the latter being most numerous in its deeper parts. Underneath the epicardium run the blood-vessels, nerves, and lymphatic vessels of the heart embedded in areolar and adipose tissue, this tissue being continuous with that which lies between the muscular bundles; the free surface of the membrane is covered by serous epithelium.

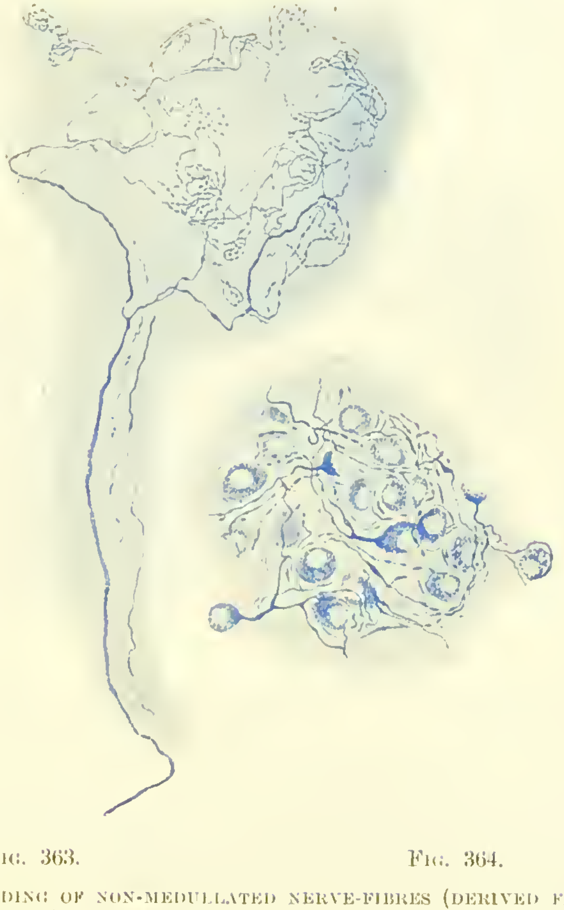

Fig. 363. Fig. 364.

Fig. 363.—Ending of non-medullated nerve-fibres (derived from the sympathetic) in a small ganglion of the heart. (Dogiel.)
The ganglion cells are not represented.

Fig. 364.—A small ganglion from the heart, showing the ganglion-cells and their processes. (Dogiel.)

The **endocardium** (fig. 359, *B*) has a structure not very unlike the pericardium. It is lined by a pavement-epithelium (endothelium), like that of a serous membrane, and consists of connective tissue with elastic fibres in its deeper part, between which there may, in some parts, be found a few plain muscular fibres. Fat is sometimes met with under the endocardium.

In some animals, *e.g.* the sheep and ox, large beaded fibres are found under the endocardium. These are formed of clear cells joined both end to end and laterally, and generally containing in their centre two nuclei, whilst the peripheral part of the cell is formed of cross-striated muscular tissue; the chains of cells form the *fibres of Purkinje* (fig. 361). They appear to be cardiac cells which have undergone differentiation into striated muscle substance only at their periphery, the non-differentiated part of the cell having continued to grow until it has attained a considerable size. In man distinct fibres of Purkinje are not seen, but the innermost muscular fibres of the ventricles are larger than those which lie more externally: they also undergo development somewhat later (J. B. MacCallum).

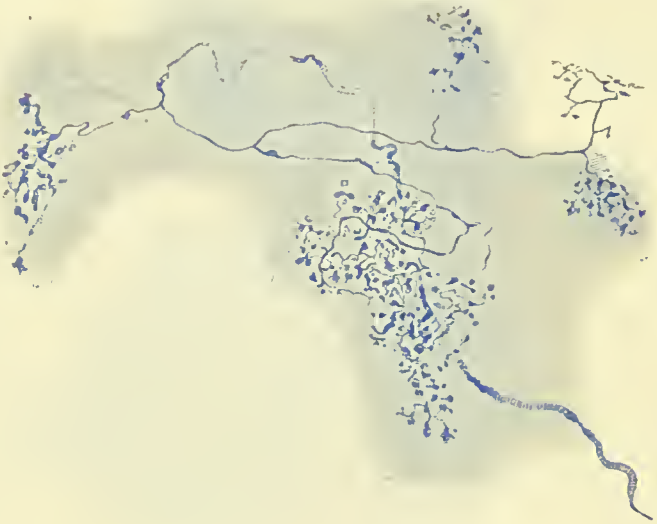

Fig. 365.—Termination of an afferent nerve-fibre in the endocardium. (A. S. Dogiel.)

A muscular bundle which shows less differentiation than the rest of the cardiac muscle has been described by W. His, junr., Stanley Kent, and others, running in the septum and affording a bridging connection between the muscle of the auricles and that of the ventricles. This *auriculo-ventricular bundle* is commonly believed to serve to propagate the contractions of the auricles to the ventricles and thus to maintain their regularity of rhythm; and it is stated that when the bundle in question is severed experimentally or by disease this propagation is no longer possible, and the ventricles in consequence beat with a much slower rhythm than the auricles. The accuracy of this statement is, however, denied by Kronecker, who regards the regularity of the cardiac contractions as a function, not of the muscular substance of the heart, but of the nerve fibres, which are distributed to every part of the myocardium, and which are also found accompanying this bundle.

The **valves** of the heart are formed of folds of endocardium strengthened by fibrous tissue (fig. 360). This tissue forms a thickening near the free edge of the valve (*c′*). At the base of the auriculo-ventricular valves the muscular tissue of the auricle may be found passing a short distance into the valve. In the fœtus these valves are at first entirely muscular.

The **nerves** of the heart are seen in sections underneath the epicardium of both auricles and ventricles; in the former situation they are connected at intervals with small ganglia (fig. 359, A, *g*; figs. 362 to 364). The axons of the ganglion-cells pass to the muscular substance, and after dividing into fine fibrils, end in enlarged extremities, which are applied directly to the muscular fibres (fig. 268). Other medullated nerve-fibres, which are probably afferent, terminate in complex ramifications in the endocardium (fig. 365) (Smirnow, A. S. Dogiel).

The **blood-vessels** of the heart are very numerous, and the veins thin-walled, retaining the capillary structure (endothelium only) in vessels of as much as 0·25 mm. in diameter. They are accompanied by numerous **lymph-vessels**, which also form plexuses under the cardiac pericardium and endocardium. The lymphatics appear to be in free communication with the spaces of the interstitial connective tissue between the muscle fibres.

LESSON XXVII.

THE TRACHEA AND LUNGS.

1. In sections of the trachea and larynx, notice the epithelium, the basement-membrane (of some thickness in the human trachea), the lymphoid tissue of the mucous membrane, the elastic tissue external to this, and lastly, the fibrous membrane containing the cartilages. In the mucous membrane and submucous areolar tissue look for sections of mucous glands, ducts of which may be seen opening on the surface. At the back of the trachea notice the plain muscular fibres transversely arranged ; there may be larger mucous glands external to these.

2. In sections of lung notice the sections of the alveoli collected into groups (air-sacs). Find sections of bronchial tubes, some cut longitudinally and passing at their extremities into the alveolar passages, others cut across. In each tube notice the ciliated epithelium internally. Next to this the mucous membrane containing numerous elastic fibres and often thrown into folds ; then the layer of circular muscular fibres, and, outside this, loose fibrous tissue in which in larger bronchial tubes pieces of cartilage may be seen embedded. Small mucous glands may also be observed in the fibrous tissue sending their ducts through the other layers to open on the inner surface. Notice that the section of a branch of the pulmonary artery always accompanies a section of a bronchial tube.

In the sections of the alveoli observe the capillary vessels passing from one side to the other of the intervening septa ; and in places where the thin wall of an alveolus is to be seen in the section, the network of blood-capillaries upon it. Notice within the alveoli nucleated corpuscles which frequently contain dark particles in their protoplasm. They are amœboid cells which have migrated from the blood-vessels and lymphatics, and have taken in inhaled particles of carbon. They may pass back into the lung tissue, for similar cells are seen in this. Make a sketch of part of the wall of one or more bronchial tubes and of one or two of the alveoli.

3. In sections of a fresh lung the air-cells of which have been filled with a mixture of gelatine and nitrate of silver solution the epithelium of the alveoli may be studied. The sections are made with the freezing microtome, and mounted in glycerine, which should be warmed after the cover-glass is applied in order to melt the gelatine.

4. Mount a section of lung in which the pulmonary vessels have been injected. Study the general arrangement of the vessels with a low power, and the network of capillaries of the alveoli with a high power. Observe that the veins run apart from the arteries. Sketch the capillary network of one or two adjoining alveoli.

The Trachea.

The **trachea** or wind-pipe is a fibrous and muscular tube, the wall of which is rendered somewhat rigid by C-shaped hoops of cartilage which are embedded in the fibrous tissue. The muscular tissue, which is of the plain variety, forms a flat band, the fibres of which run transversely at the back of the tube. The trachea is lined by a *mucous membrane* (fig. 366), which has ciliated epithelium upon its inner surface (fig. 367). The epithelium-cells, which have been already described (Lesson VIII.), have goblet cells amongst them: they rest upon a thick basement-membrane. The corium of the mucous membrane consists of areolar and lymphoid tissue, and contains numerous blood-vessels and lymphatics. In its deepest part is a well-marked layer of longitudinal elastic fibres. Many small glands—mucous and mixed mucous and serous—are found in the wall of the trachea. They may lie either within the mucous membrane or in the submucous areolar tissue, or, lastly, at the back of the trachea, outside the transverse muscular fibres.

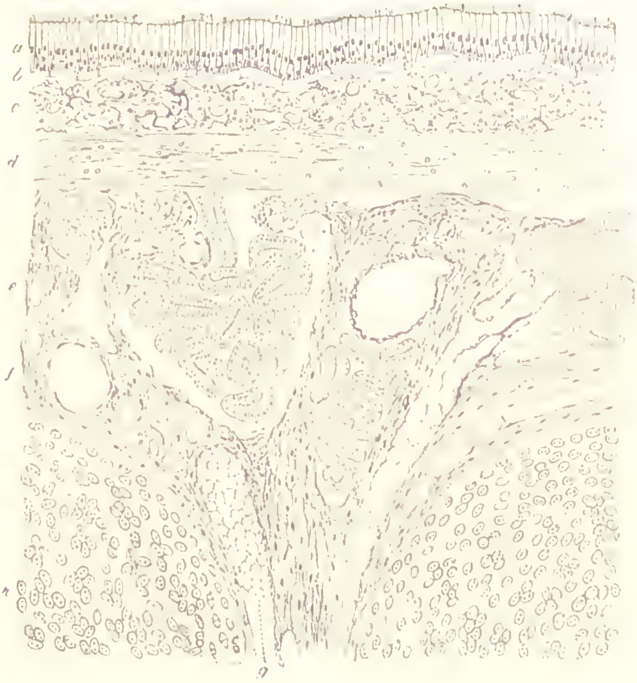

FIG. 366.—LONGITUDINAL SECTION OF THE HUMAN TRACHEA, INCLUDING PORTIONS OF TWO CARTILAGINOUS RINGS. (Klein.) Moderately magnified.

a, ciliated epithelium; *b*, basement-membrane; *c*, superficial part of the mucous membrane, containing the sections of numerous capillary blood-vessels and much lymphoid tissue; *d*, deeper part of the mucous membrane, consisting mainly of elastic fibres; *e*, submucous areolar tissue, containing the larger blood-vessels, small mucous glands (their ducts and alveoli are seen in section), fat, etc.; *f*, fibrous tissue investing and uniting the cartilages; *g*, a small mass of adipose tissue in the fibrous layer; *h*, cartilage.

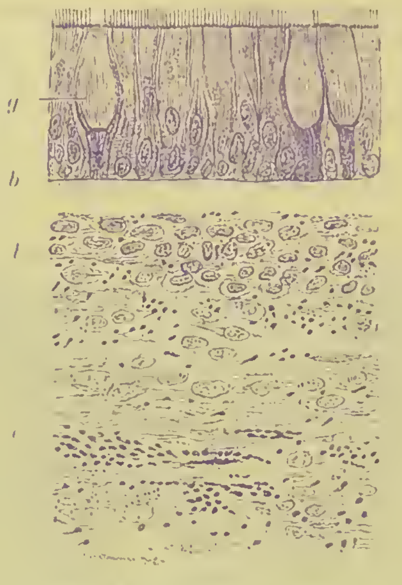

FIG. 367.—MUCOUS MEMBRANE OF LARYNX, MORE MAGNIFIED THAN FIG. 366.

g, a goblet-cell amongst the ciliated epithelium-cells ; *b*, basement-membrane ; *l*, lymphoid tissue ; *e*, elastic fibres, cut across.

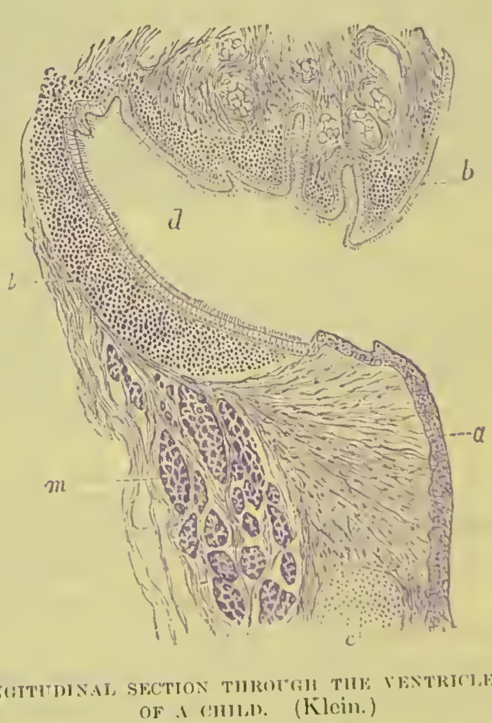

FIG. 368.—LONGITUDINAL SECTION THROUGH THE VENTRICLE OF THE LARYNX OF A CHILD. (Klein.)

a, true vocal cord ; *b*, false vocal cord ; *c*, nodule of cartilage ; *d*, ventricle of Morgagni ; *l*, lymphoid tissue ; *m*, thyro-arytenoid muscle.

The two divisions of the trachea, the *bronchi*, are precisely similar in structure to the main tube.

The **larynx** is also very like the trachea so far as the structure of the mucous membrane is concerned. It is lined by ciliated epithelium, but over the true vocal cords and upon the epiglottis, as well as here and there in the part above the glottis, stratified epithelium is found; and taste-buds may occur in this epithelium, except over the vocal cords. Numerous nerves end in the epithelium (fig. 258).

The true vocal cords are composed of fine elastic fibres.

Lymphoid tissue is especially abundant in the mucous membrane of the ventricle of Morgagni (fig. 368, *d*), and a large number of mucous glands open into this cavity and into that of the sacculus, which communicates with it.

The cartilages of the trachea and the thyroid, cricoid and arytenoid cartilages of the larynx are hyaline; all these are liable to ossify as age advances. The epiglottis and the cartilages of Santorini and of Wrisberg are composed of elastic fibro-cartilage. This is also the case with the uppermost part of the arytenoid and the tip of the vocal process of the same cartilage.

THE LUNGS.

The lungs are formed by the ramifications of the *bronchial tubes* and their terminal expansions, which form groups or lobules of sacculated dilatations (*air-sacs, infundibula*), beset everywhere with small irregularly hemispherical or cubical bulgings, known as the *air-cells* or *pulmonary alveoli*.

The **bronchial tubes** (figs. 369, 370, 371) are lined (except the terminal bronchi) by ciliated epithelium which rests on a basement membrane. External to this is the corium of the mucous membrane, containing a large number of longitudinal elastic fibres and some lymphoid tissue. Outside this again is a complete layer of plain muscular fibres encircling the tube. Next comes a loose fibrous layer in which, in the larger tubes (fig. 369), small plates of cartilage are embedded. Mucous glands are also present in this tissue.

The extremities of the bronchial tubes expand into passages, the *respiratory bronchioles*, which give off branches, termed *alveolar ducts* or *terminal bronchioles*. The walls of these are beset with alveoli. The terminal bronchioles lead through nearly spherical alveolated dilatations (the *atria*) into a number of blind and often funnel-shaped diverticula completely covered with alveoli; these are known as the *infundibula, alveolar sacs* or *air-sacs* (Waters). The arrangement of these parts, according to the investigations of W. S. Miller, is as follows: Two or more *air-sacs*, or groups of *alveoli*, open into a common chamber (*atrium*), and three to six atria into an *alveolar duct* or *terminal bronchiole*. The latter open into the respiratory bronchioles,

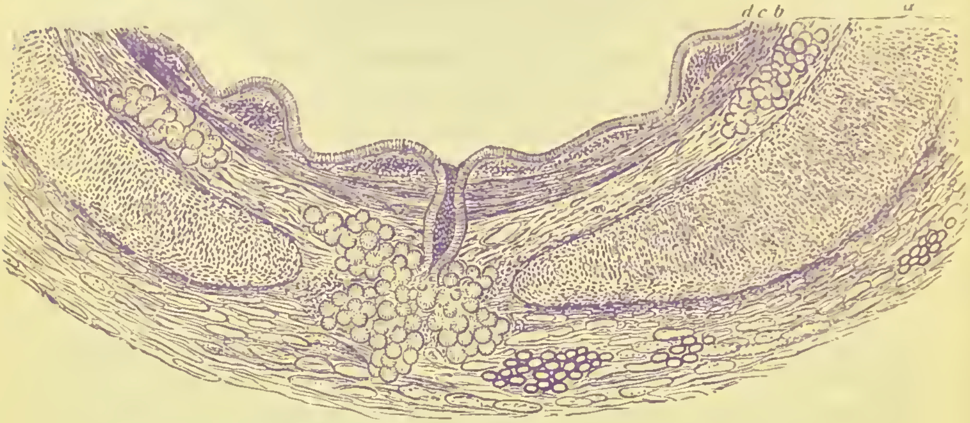

Fig. 369.—Portion of a transverse section of a bronchial tube, human, 6 mm. in diameter. (F. E. Schultze.) Magnified 30 diameters.

a, cartilage and fibrous layer with mucous glands, and, in the outer part, a little fat; in the middle, the duct of a gland opens on the inner surface of the tube; *b*, annular layer of involuntary muscular fibres; *c*, elastic layer, the elastic fibres in bundles which are seen cut across; *d*, columnar ciliated epithelium.

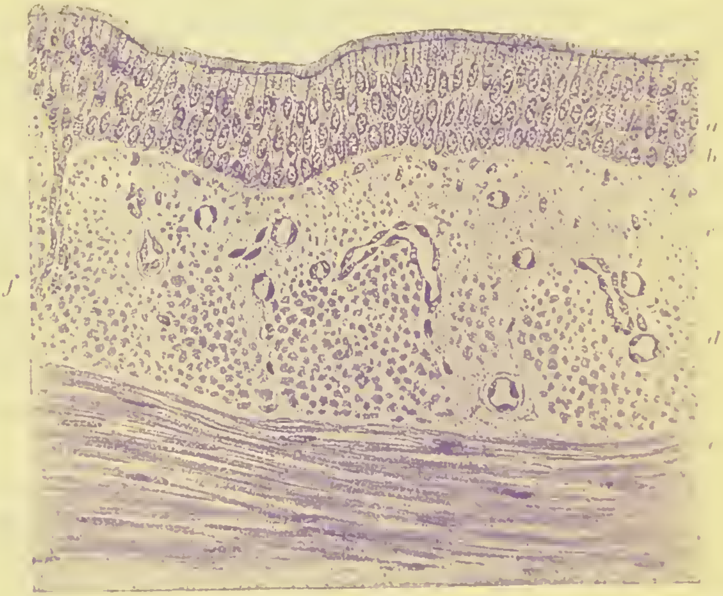

Fig. 370.—Section of part of a bronchial tube. Magnified 200 diameters.

a, ciliated epithelium; *b*, basement-membrane; *c*, superficial part of mucous membrane, with fine elastic fibres; *d*, deeper part with numerous coarser fibres; *e*, plain muscle of bronchus; *f*, duct of gland passing through mucous membrane.

which are expanded continuations of the smallest bronchi. All of these, except the last named, are beset with alveoli.

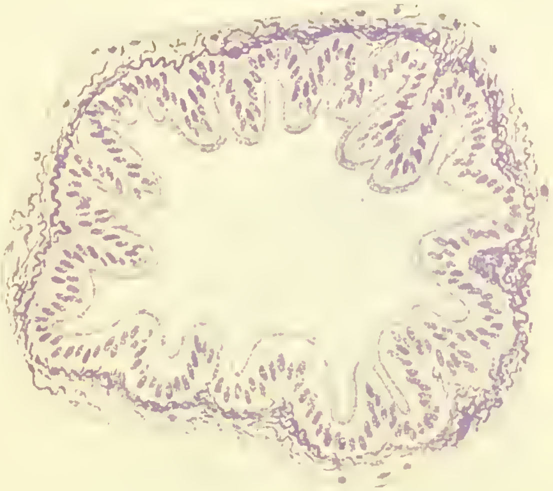

Fig. 371.—Section of a small bronchial tube, human. (Sobotta.) × 280.
The elastic fibres of the mucous membrane are stained.

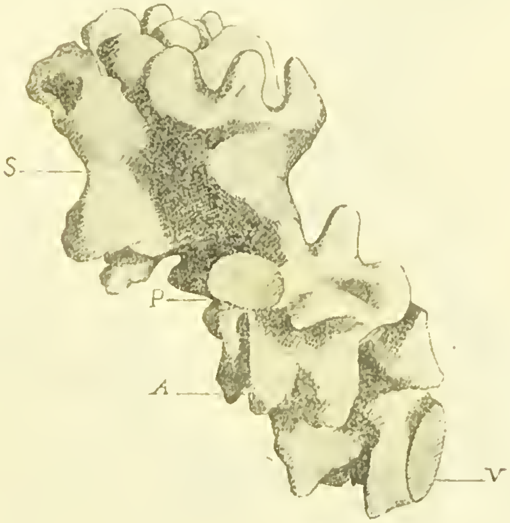

Fig. 372.—Cast of lobule of dog's lung showing a single infundibulum or air-sac. (W. S. Miller.)

A, atrium; *V*, vestibule or end of alveolar duct leading to atrium; *S*, air-sac (infundibulum); *P*, section of the neck of a second air-sac (cut away). The irregular projections on the atrium and infundibula are the alveoli.

The epithelium changes in character in the alveolar ducts; from columnar and ciliated it becomes cubical and non-ciliated, and there are patches of the respiratory epithelium (see below) not only in the alveoli which beset the ducts, but also elsewhere in their wall. The plain muscular tissue of the bronchiole is continued on the walls of the alveolar ducts, but not on those of the atria, although some occur round the mouths of the atria and even of the alveoli.

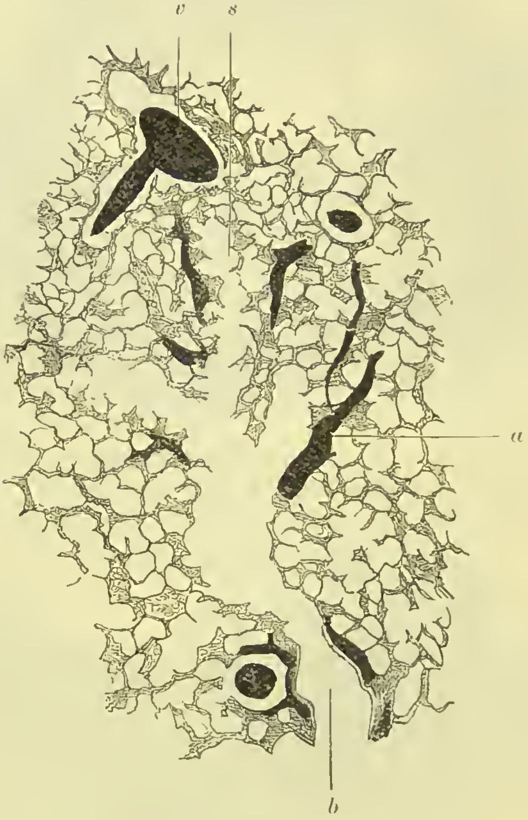

FIG. 373.—SECTION OF LUNG (HUMAN), LOW POWER. (F. Merkel.)

a, artery ; *v*, vein ; *b*, respiratory bronchiole opening into alveolar duct, which communicates with groups of alveoli (air-sacs, *s*).

The **alveoli** are lined by large irregular flattened cells (fig. 375), which form an extremely delicate layer (respiratory epithelium), separating the blood-capillaries from the air within the alveoli. Amongst the flattened cells are here and there groups of smaller and thicker (cubical) epithelium-cells. The capillary network of the alveoli is very close (fig. 376), and the capillary vessels of adjoining alveoli are in complete continuity, the vessels passing first to one side and then to the other of the septa which separate the adjacent alveoli. Outside the epithelium a thin layer of connective tissue (basement-membrane ?) forms the wall of each alveolus. Elastic fibres are numerous around

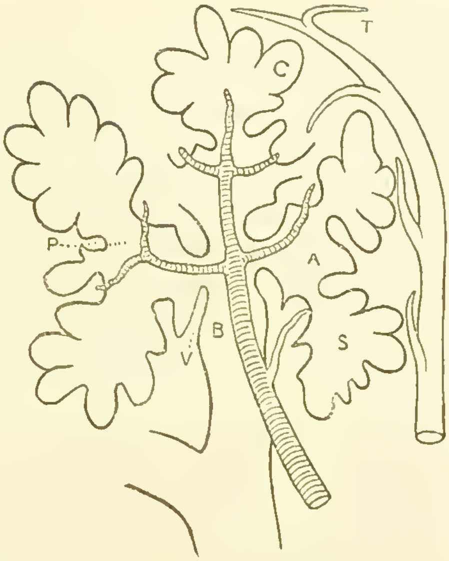

Fig. 374.—Diagram of the ending of a bronchial tube. (W. S. Miller.)

B, terminal bronchiole; V, vestibule; A, atrium; S, air-sac (infundibulum); C, air-cell (alveolus); P, ending of pulmonary arteriole; T, commencement of pulmonary venule.

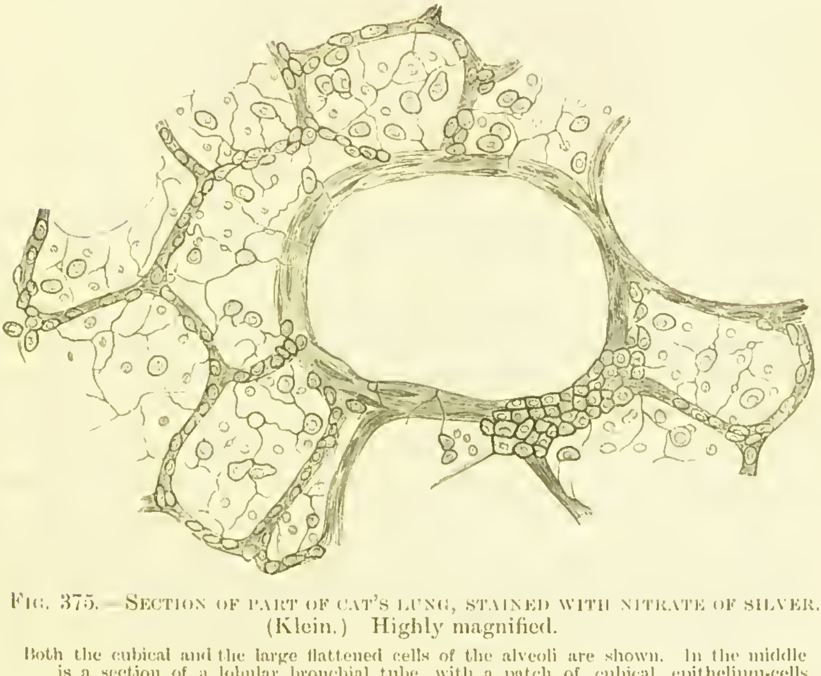

Fig. 375.—Section of part of cat's lung, stained with nitrate of silver. (Klein.) Highly magnified.

Both the cubical and the large flattened cells of the alveoli are shown. In the middle is a section of a lobular bronchial tube, with a patch of cubical epithelium-cells at one side.

the mouths of the alveoli, and a certain number course over the wall of each alveolus.

Blood-vessels.—Branches of the pulmonary artery accompany the bronchial tubes to be distributed to the capillary networks upon the alveoli, from which the blood is returned by the pulmonary veins. An arteriole runs with each terminal bronchiole, and, dividing into as many branches as there are atria, is distributed to the capillary networks of all the air-cells with which the bronchiole is connected (Miller). From these networks one or two venules collect the blood, usually coursing (independently of the arteriole) on the outer border of the group of infundibula, and unite with other venules to form efferent veins. The venules of the superficial lobules are connected with a vascular network at the surface of the lung underneath the pleura. This network is also supplied from the bronchial arteries. The veins, pursuing a separate course through the tissue of the lung, join with others to form larger vessels which pass to the root of the lung. Branches from the bronchial arteries are distributed to the walls of the bronchial tubes, and to the connective tissue of the lung, including that of the pleura. Bronchial veins accompany the bronchial arteries to the larger tubes, but most of the blood brought to the lungs by the bronchial arteries is returned by the pulmonary veins. Connective tissue intervenes everywhere in small quantity between the infundibula (interstitial tissue), and forms a distinct layer, containing

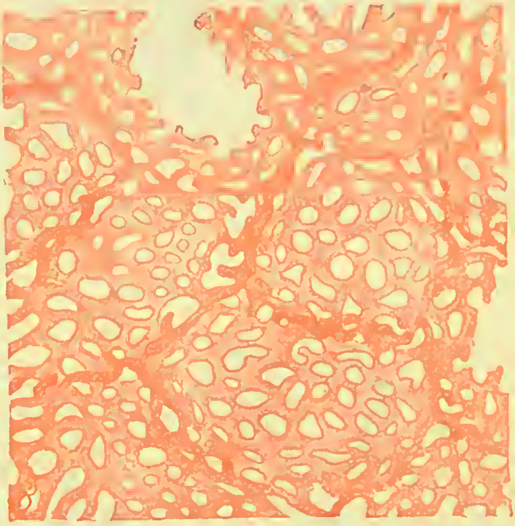

FIG. 376.—SECTION OF INJECTED LUNG OF RABBIT, INCLUDING SEVERAL CONTIGUOUS ALVEOLI. (Szymonowicz.) Magnified 300 diameters.

much elastic tissue, covering the surface of the lung underneath the serous membrane (subserous tissue). In some animals (*e.g.* guinea-pig) the subserous layer contains plain muscular tissue, which is especially developed near the lung-apex; it has not been detected in man.

The **lymphatics** of the lung accompany the bronchial tubes, the branches of the pulmonary artery, and the branches of the pulmonary vein; and they also form a network in the pleura. The atria and air-sacs have no lymphatics in their walls (Miller). The bronchial lymphatics are less superficial than the corresponding blood-vessels. The larger tubes have two plexuses, one within the other outside the cartilages. The smaller have only one set. The lymphatics of the bronchi are connected with those of the arteries and veins by lateral branches curving off at the divarications of the tubes; at these points there is usually an accumulation of lymphoid tissue. The larger arteries and veins have two accompanying lymphatics, the smaller only one. All the lymphatics tend towards the hilus, and enter lymphatic glands at the root of the lung. Those in the pleura have been said to communicate, by means of stomata between the epithelial cells of the serous membrane, with the cavity of the pleura; this connection is denied by Miller. The lymphatics of the pleura are furnished with numerous valves.

The **pleura**, which covers the surface of the lung, has the usual structure of a serous membrane (p. 230 and fig. 298). It is provided with a special network of blood-vessels, which is supplied partly from the pulmonary vessels of the superficial lobules, partly from the bronchial arteries.

The lung is developed in the same manner as a secretory gland, to which, up to a certain period of formation, it bears a close resemblance. Its alveoli correspond with those of a racemose gland, and the cells which line them are, prior to the introduction of air, of some thickness and of protoplasmic nature. It is only after the organ has come into use for respiration that they acquire the thin flattened scaly appearance which most of them present in the adult lung.

LESSON XXVIII.

STRUCTURE AND DEVELOPMENT OF THE TEETH.

1. Study first with the low power and afterwards with the high power a longitudinal section of a human tooth which has been prepared by grinding. It is better to purchase this specimen, for the process of preparation is difficult and tedious without the aid of special apparatus. Examine carefully the enamel, the dentine, and the cement. The dark appearance of the dentinal tubules is due to their containing air in the dried specimen. Measure the diameter of the enamel prisms and of some of the dentinal tubules. Make sketches from each of the tissues.

2. Section of a tooth *in situ*, which has been decalcified after fixation, and stained. In this section the mode of implantation of a tooth, as well as the structure of the pulp, can be made out. Make a general sketch under a low power, and under a high power draw a small piece of the pulp showing the processes of the odontoblasts extending into the dentinal tubules.

3. The development of the teeth and the formation of their tissues are studied in sections made across the snout and lower jaw of fœtal and young animals. The preparations may be stained in bulk or the individual sections may be stained.

The Teeth.

A **tooth** consists in man of three calcified tissues; *enamel*, which is of epithelial origin, *dentine*, and *cement* or *crusta petrosa*. The dentine forms the main substance of a tooth, the enamel covers the crown, and the cement is a layer of bone which invests the root (figs. 377 to 379).

Enamel is formed of elongated hexagonal *prisms* (figs. 380, 381), which are set vertically, or with a slight curvature, upon the surface of the dentine. They are marked at tolerably regular intervals with slight transverse shadings producing an indistinct cross-striated appearance. Sometimes coloured lines run through the enamel across the direction of its prisms. The enamel prisms have when first laid down a fibrous structure, but this becomes obscured after their calcification is complete. C. Tomes has shown that the enamel of the fully formed tooth contains only an extremely minute proportion of animal matter: practically it is wholly composed of earthy matter (lime salts).

Dentine is constituted of a hard dense substance like bone, but containing no Haversian canals or lacunæ. It is pierced everywhere by fine canaliculi (*dentinal tubules*, fig. 382), radiating outwards from a central cavity which, during life, contains the pulp. The tubules branch at acute angles as they pass outwards; their branches become gradually finer towards the periphery of the dentine. The dentinal tubules are occupied by processes of the odontoblasts (p. 305).

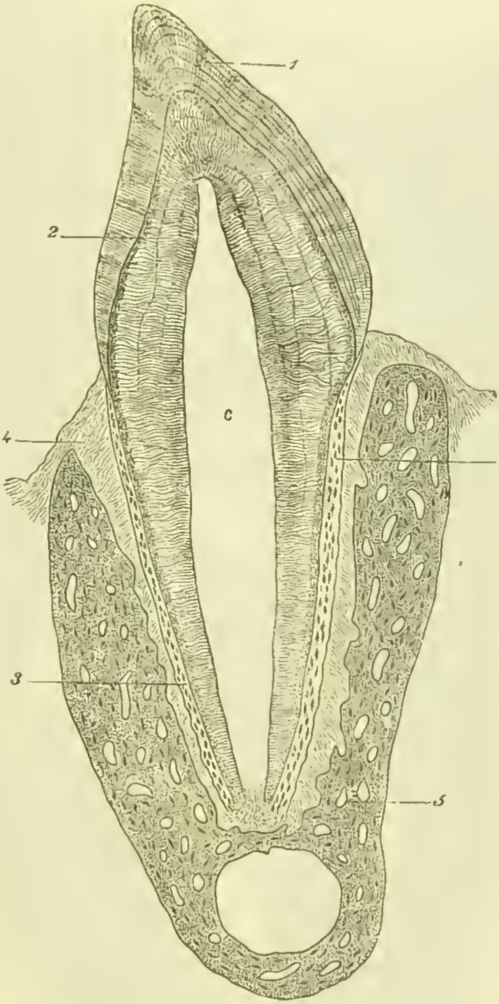

Fig. 377.—Vertical section of a tooth in situ. (Waldeyer.)

c, is placed in the pulp-cavity, opposite the cervix or neck of the tooth; the part above is the crown, that below is the root (fang). *1*, enamel with radial and concentric markings; *2*, dentine with tubules and incremental lines; *3*, cement or crusta petrosa, with bone corpuscles; *4*, dental periosteum; *5*, bone of lower jaw.

The tubules have a proper wall of their own, which can be isolated by steeping a section of tooth in strong hydrochloric acid. In the living tooth they are occupied by protoplasmic fibres (Tomes' fibres), which are prolonged from the superficial cells of the pulp.

The intertubular substance appears for the most part homogeneous, but here and there indications can be seen in it of a globular formation. This is especially the case near the surface of the dentine,

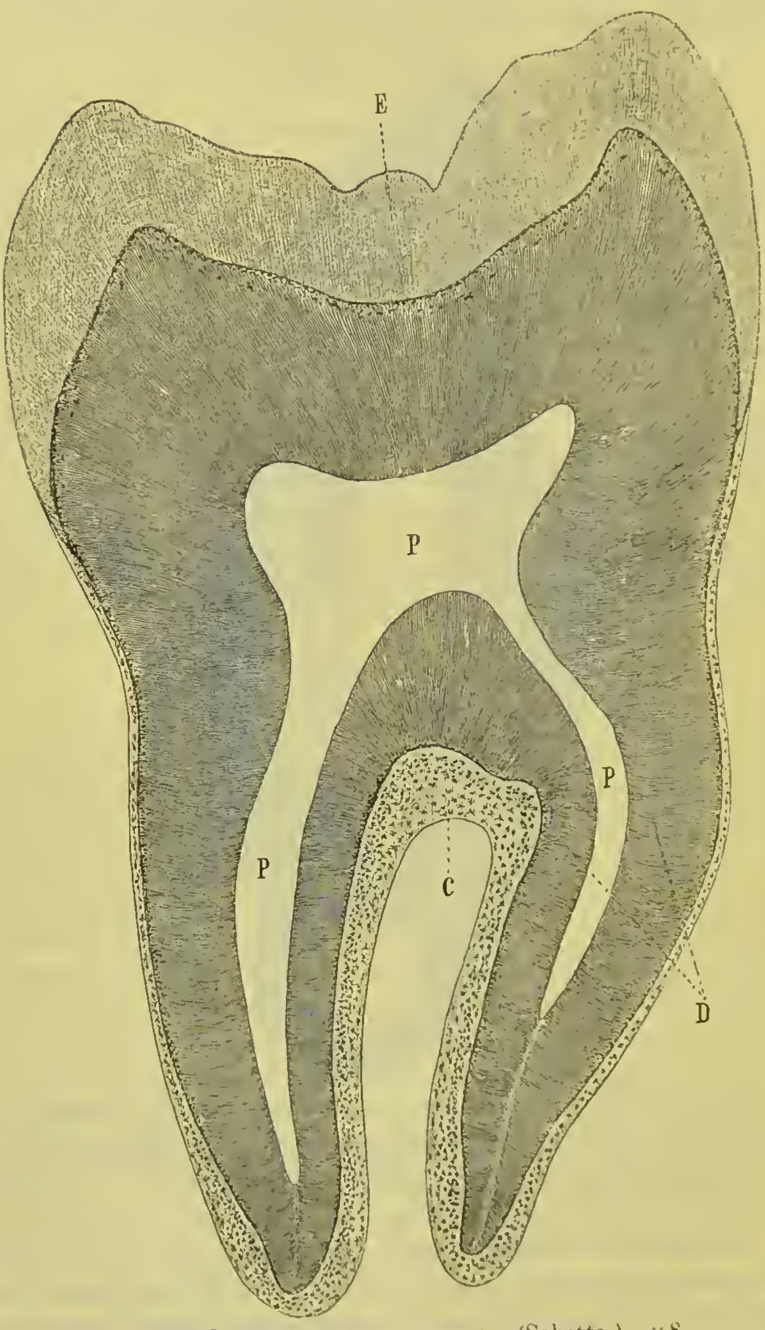

FIG. 378.—SECTION OF MOLAR TOOTH. (Sobotta.) ×8.
E, enamel; D, dentine; C, cement; P, pulp cavity.

where the globular deposit and the interglobular spaces may produce a granular appearance (*granular layer*, fig. 379, G), and also in the course of certain lines or clefts which are seen traversing the dentine across the direction of the tubules (*interglobular spaces, incremental lines,* fig. 377, shown magnified in fig. 384). After decalcification the dentine can be separated into lamellæ along these incremental lines.

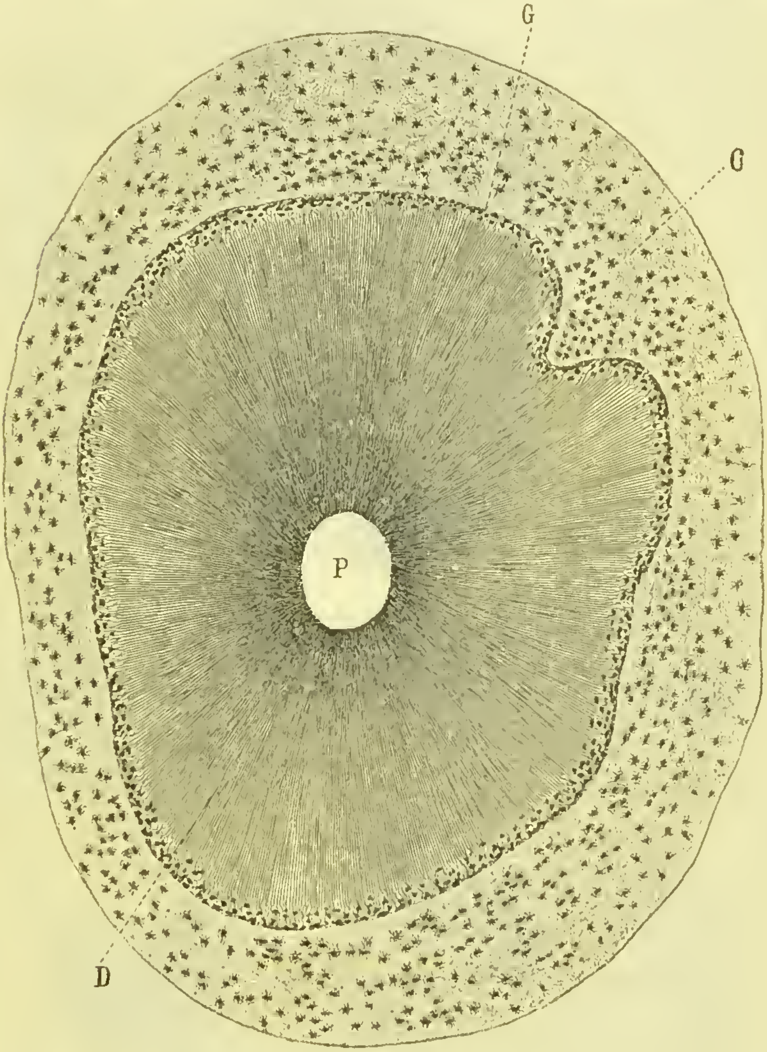

FIG. 379.—CROSS-SECTION OF ROOT OF CANINE TOOTH, HUMAN. (Sobotta.) × 25.

D, dentine ; G, its granular layer ; C, cement ; P, pulp cavity.

The animal matter of dentine resembles bone and the connective tissues generally in having its ground-substance pervaded by fibres which yield gelatine on boiling. These fibres, which have been especially investigated by v. Ebner and by Mummery, are difficult of demonstration in the fully calcified dentine; but in developing dentine

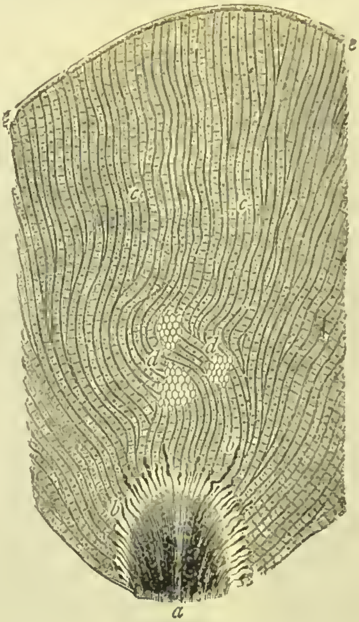

FIG. 380.—SECTION THROUGH THE ENAMEL OF A TOOTH. Magnified 200 diameters. (Rauber.)

a, projection of dentine, showing some of its tubules, *b*, penetrating into the enamel: *c*, *c*, enamel fibres cut longitudinally; *d*, *d*, prisms cut transversely; *e*, cuticle of the enamel.

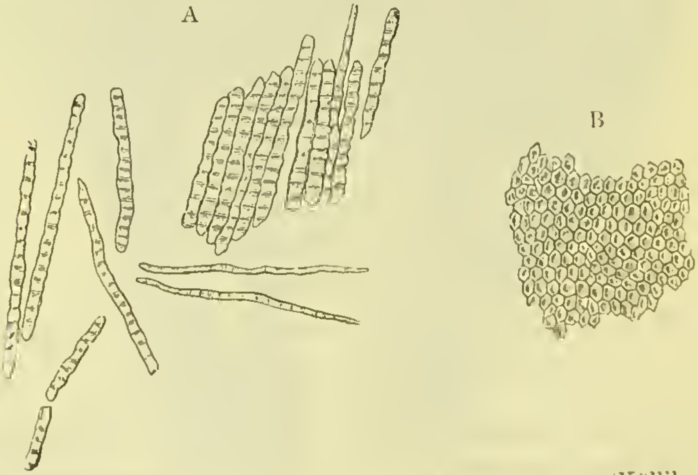

FIG. 381.—ENAMEL PRISMS. Magnified 350 diameters. (Kölliker.)

A, Fragments and single fibres of the enamel, isolated by the action of hydrochloric acid. B, Surface of a small fragment of enamel, showing the hexagonal ends of the fibres.

and in dentine which is attacked by caries, they are more easily shown. They run for the most part parallel to the surface.

The **pulp** (fig. 385) consists of a soft, somewhat jelly-like, connective tissue, containing many branched cells, a network of blood-vessels, and many nerve-fibres which pass into the pulp-cavity along with the blood-vessels by a minute canal at the apex of the fang. The superficial cells of the pulp form an almost continuous layer, like an epithelium (fig. 385, *Od*, *Od'*). They are known as *odontoblasts*, from having been

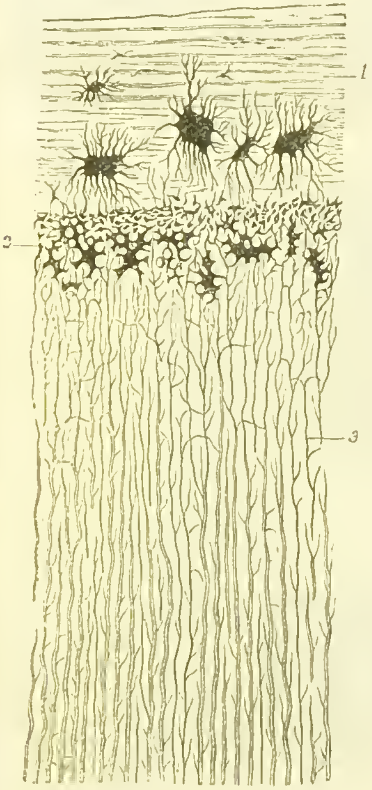

Fig. 382.

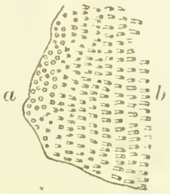

Fig. 383.

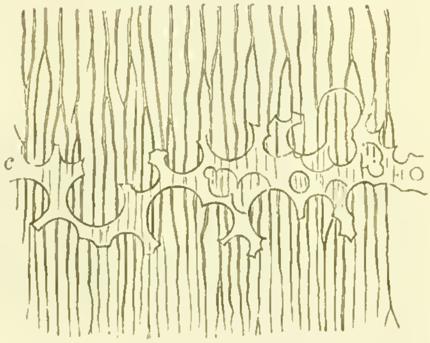

Fig. 384.

Fig. 382.—Section of fang, parallel to dentinal tubules. Magnified 300 diameters. (Waldeyer.)

1, cement, with large bone lacunæ and indications of lamellæ; *2*, granular layer of Purkinje (interglobular spaces); *3*, dentinal tubules.

Fig. 383.—Sections of dentinal tubules. Magnified about 300 diameters. (Fraenckel.)

a, cut across; *b*, cut obliquely.

Fig. 384.—A small portion of dentine with interglobular spaces. Magnified 350 diameters. (Kölliker.)

c, portion of incremental line formed by the interglobular spaces, which are here filled up by a transparent material.

concerned in the formation of the dentine. The nerve fibres are said to pass eventually between the odontoblasts and to end in arborisations close to the dentine, but they have not been followed into the dentinal tubules.

The **crusta petrosa** (figs. 379, 382) is a layer of lamellated bone, including lacunæ and canaliculi, but without Haversian canals, at least normally, in the human teeth. It is covered with periosteum (*dental periosteum*), which also lines the socket, and serves to fix the tooth securely.

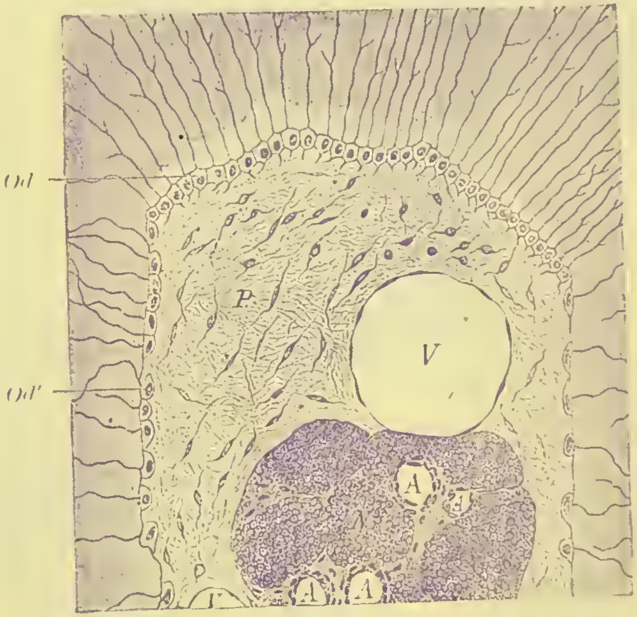

Fig. 385.—Section across the root of a young tooth showing the pulp in situ. (Röse.)

P, pulp; *V*, *V*, veins; *A*, *A*, *A*, arterioles; *N*, nerve bundles; *Od*, columnar odontoblasts still depositing dentine; *Od'*, flattened odontoblasts which have ceased to form dentine.

Formation of the teeth.—The teeth are developed somewhat similarly to the hairs. A continuous thickening of the epithelium occurs along the line of the gums, and grows into the corium of the mucous membrane (*common dental germ* or *dental lamina*, fig. 386, A). At regular intervals there is yet a further thickening and growth from the common germ into the tissue of the mucous membrane, each of these special rudiments, which are ten in number, swelling out below into a flask-shaped mass of cells, the *special dental germ* (fig. 386, B) of a milk-tooth. The intermediate parts of the dental lamina long remain, forming a common epithelial strand uniting the several special dental germs to one another and to the epithelium covering the gum (fig. 386, C, D, *f*). A vascular *papilla* is continued from the corium into the bottom of each special

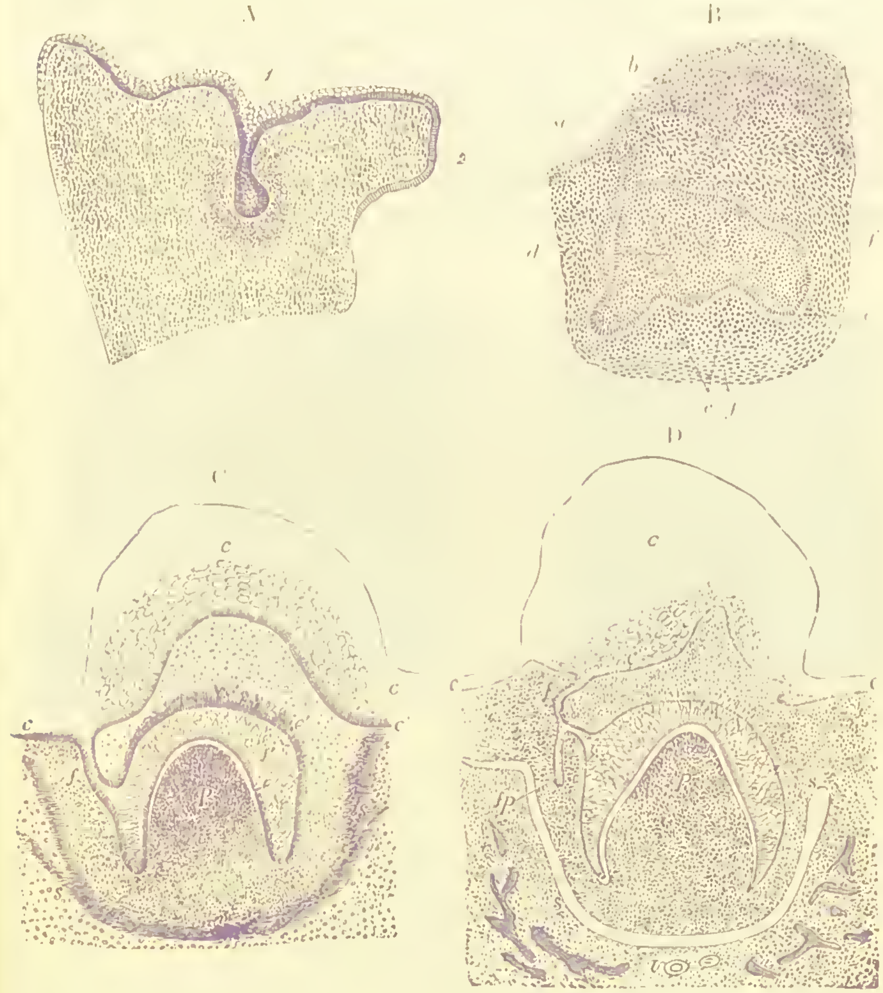

Fig. 386.

A. Section across the upper jaw of a fœtal sheep, 3 centimeters long. (Waldeyer.)

1, common dental lamina dipping down into the mucous membrane where it is half surrounded by a horseshoe-shaped more dense-looking tissue, the germ of the dentine and dental sac; *2*, palatine process of the maxilla.

B. Section from fœtal calf similar to that shown in A, but passing through one of the special dental germs here becoming flask-shaped. (Röse.)

a, epithelium of mouth, thickened at *b*, above special dental germ; *c*, papilla; *d*, special dental germ; *e*, enamel epithelium; *f*, dental sac.

C and D. Sections at later stages than A and B, the papilla having become formed and having become partly surrounded by the epithelial germ. (Kölliker.)

c, epithelium of gum, sketched in outline; *f*, neck of dental germ; *f′*, enamel organ; *e*, its deeper columnar cells; *e′*, projections into the corium; *p*, papilla; *s*, dental sac forming. In D, the dental germ (*fp*) of the corresponding permanent tooth is seen.

germ (fig. 386, C, D, *p*); this papilla has the shape of the crown of the future tooth. Each special dental germ, with its included papilla, presently becomes almost entirely cut off from the epithelium of the mouth, and surrounded by a vascular membrane—the *dental sac*. The papilla becomes transformed into the dentine and pulp of the future tooth, and the enamel is deposited upon its surface by the epithelial cells of the dental germ. The root of the tooth, with its covering of cement, is formed at a later period, when the tooth is beginning to grow up through the gum, by a gradual elongation of the

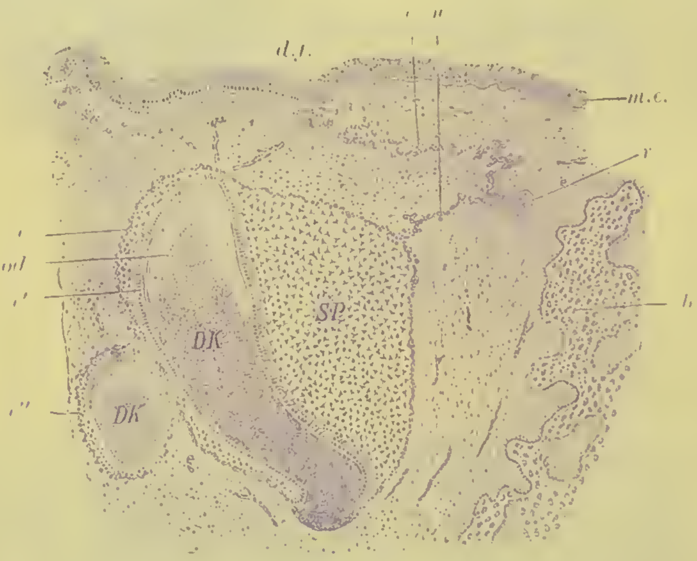

FIG. 387.—SECTION OF A DEVELOPING INCISOR TOOTH OF A HUMAN EMBRYO. (Röse.) THE SECTION ALSO INCLUDES THE GERM OF THE ADJACENT TOOTH.

DK, dental papilla; *od*, odontoblasts; *b*, bone of jaw; *e*, *e'*. outer and inner layers of enamel-organ; *S.P.*, enamel pulp; *d.f.*, dental furrow; *c*, remains of common dental germ or lamina; *n*, neck or bridge of cells connecting this with the enamel-organ; *m.e.*, mouth-epithelium; *e''*, enamel organ of adjacent tooth-germ; *r*, reserve germ of permanent tooth.

base of the papilla. The shaping of this into the form of the root is determined by a growth of the epithelium of the edge of the enamel germ, which extends in the form of a fold (the *epithelial sheath* of v. Brunn) towards the future apex of each fang.

Previously to the deposition of the enamel, the dental germ undergoes a peculiar transformation of its previously polyhedral epithelium-cells into three layers of modified cells. One of these is a layer of columnar cells (*ameloblasts*, fig. 388, *a*), immediately covering the surface of the dentine. The enamel-prisms are produced by a fibrous formation (fig. 389, *f*) followed by a deposition of calcareous salts; these changes taking place altogether external to the cells (or, as some hold, by a direct calcification of their protoplasm). The cells next to the dental sac form a single layer of cubical epithelium (fig. 387, *e*), and nearly all the other cells of the dental germ become transformed into branching corpuscles (fig. 387, *SP*; fig. 388, *p*) communicating by their processes, and thus forming a continuous network. The dental germ, after it is thus modified, is known as the *enamel organ.*

The *dentine* of the tooth is formed by calcification of the surface of the papilla. At this surface there is a well-marked layer of odontoblasts (fig. 390, *od*; fig. 391, *c*), and these produce a layer of fibrillated dentinal matrix which forms a sort of cap to the papilla, and which soon becomes calcified by the deposition of globules of calcareous matter. Processes of the odontoblasts remain in the dentine as it is forming, and thus the dentinal tubules are produced. Subsequently other layers of dentine are formed within the first by a repetition of the same process, and in this way the papilla gradually becomes calcified. A part, however, remains unaltered in the centre of the tooth, and with its covering of odontoblasts forms the pulp.

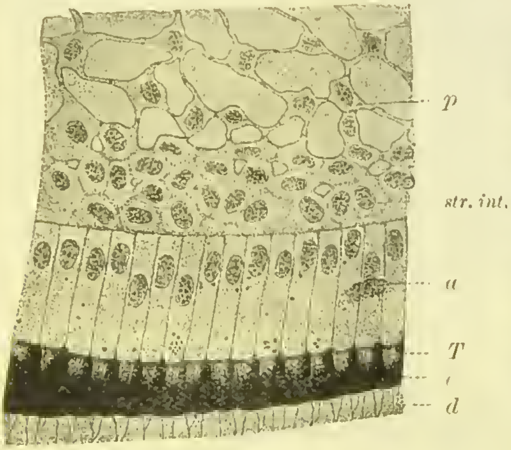

Fig. 388.

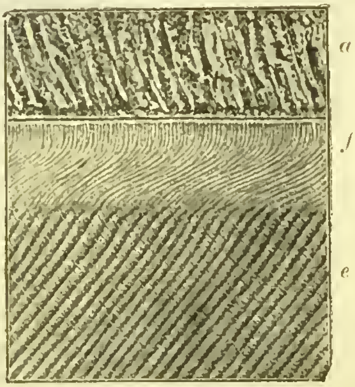

Fig. 389.

Fig. 388.—Section showing the structure of the part of the enamel organ which lies next to the dentine. (Röse.)

d, dentine; *e*, newly formed enamel stained black by osmic acid; *T*, Tomes' processes from the ameloblasts, *a*; *str. int.*, stratum intermedium of enamel organ; *p*, branched cells of enamel pulp.

Fig. 389.—Developing enamel showing ameloblasts and the fibrous substance produced by these cells, which forms the basis of the enamel prisms. (From a photograph by Leon Williams.)

a, portions of the ameloblasts; *f*, fibrous basis of enamel prisms; *e*, calcified part of enamel.

The ten milk-teeth are formed in each jaw in the manner described. These, however, become lost within a few years after birth, and are replaced by permanent teeth in much the same way that a new succession of hair occurs. A small outgrowth takes place at an early period from the dental germ close to each of the milk-teeth (fig. 386, D, *fp*), and this eventually becomes the germ of the corresponding permanent tooth. It gradually enlarges, acquires a papilla, forms an enamel organ: in short, passes through the same phases of development as

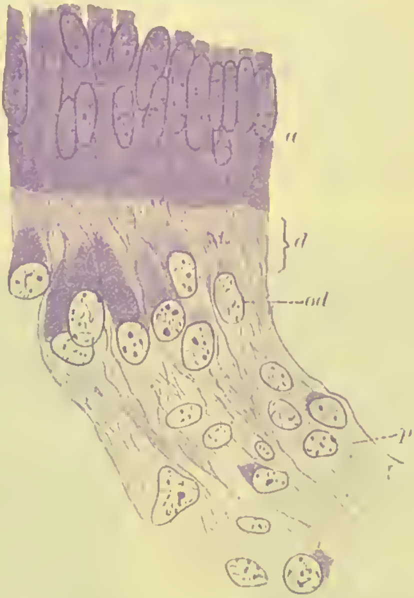

FIG. 390.—PART OF A SECTION OF DEVELOPING TOOTH OF PIG. (v. Korff.)

a, ameloblasts; *d*, fibres of the first formed layer of dentine; *od*, odontoblasts; *p*, pulp. The fibres of the pulp are seen to be in continuity with those which enter into the formation of the dentine.

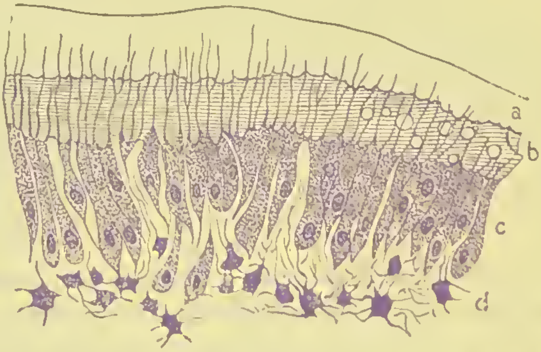

FIG. 391.—PART OF SECTION OF DEVELOPING TOOTH OF YOUNG RAT, SHOWING THE MODE OF DEPOSITION OF THE DENTINE. Highly magnified.

a, outer layer of fully calcified dentine; *b*, uncalcified matrix, with a few nodules of calcareous matter; *c*, odontoblasts with processes extending into the dentine; *d*, pulp. The section being stained, the uncalcified matrix is coloured, but not the calcified part.

the germ of the milk-tooth; and when the milk-tooth drops out of the jaw in consequence of the absorption of its roots (by osteoclasts) the permanent tooth grows up into its place.

There are six permanent teeth in each jaw which do not succeed milk-teeth; these are the permanent molars. They are developed from an extension backwards on each side of the jaw of the original epithelial thickening or common dental germ and by the downgrowth from this into the corium of three successive special germs at comparatively long intervals of time. Within these the tissues of the permanent molars become formed in a manner exactly similar to that in which the milk-teeth are developed.

LESSON XXIX.

THE TONGUE AND THE GUSTATORY ORGANS. THE MUCOUS MEMBRANE OF THE MOUTH. THE PHARYNX ŒSOPHAGUS.

1. Sections of the tongue vertical to the surface, stained with hæmatoxylin and eosin. The sections should be taken from different parts and include all three kinds of papillæ.

2. Sections of injected tongue.

3. Sections of the papilla foliata of the rabbit, stained with hæmatoxylin and eosin to show the taste-buds *in situ*.

The cells composing the taste-buds are studied by teasing osmic preparations of the papilla foliata; the nerve-endings are seen in sections of papillæ foliatæ which have been treated by Golgi's osmic-bichromate-silver method.

4. Sections of the pharynx and of the œsophagus stained with hæmatoxylin and eosin.

The **tongue** is mainly composed of striated muscular fibres, running some longitudinally, and others transversely. It is covered by a mucous membrane, the epithelium of which, like that of the rest of the mouth, is thick and stratified, and conceals microscopic papillæ (fig. 392) like those of the skin. Besides these, the upper surface of the organ is covered with larger papillæ, which give it a rough appearance. These, which are termed the *lingual papillæ*, are of three kinds: (1) About twelve or thirteen comparatively large circular projections, each of which is surrounded by a narrow groove (fossa), external to which the mucous membrane is raised above the general level (vallum) (fig. 393). These papillæ form a V-shaped line towards the back of the tongue; they receive filaments of the glosso-pharyngeal nerve, and have taste-buds in the epithelium which covers their sides, and in that of the side of the vallum. They are known as the *circumvallate papillæ*. (2) All the rest of the papillary surface of the tongue is covered by *conical papillæ*, so named from the conical pointed cap of epithelium which is borne by each; sometimes this cap is fringed with fine epithelial filaments, when they are termed *filiform* (fig. 394). (3) Scattered here and there amongst the conical papillæ are other larger papillæ, the *fungiform* (fig. 395). These are very vascular, and lie partly embedded in little depressions of the mucous membrane.

Small tubular glands may be seen between the superficial muscular fibres sending their ducts to the surface. Most of them secrete mucus, but those which open into the trenches of the circumvallate papillæ,

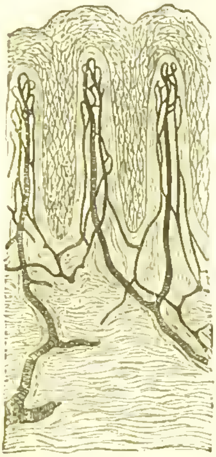

Fig. 392.—Section of mucous membrane of mouth, showing three microscopic papillæ and stratified epithelium. The blood-vessels have been injected. (Toldt.)

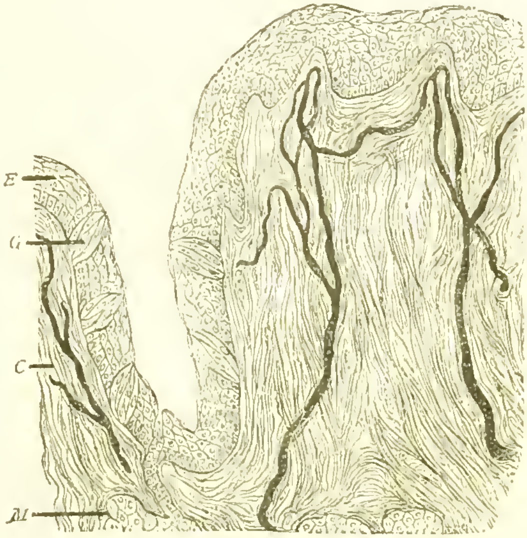

Fig. 393.—Section of circumvallate papilla, human. The figure includes one side of the papilla and the adjoining part of the vallum. Magnified 150 diameters. (Heitzmann.)

E, epithelium; *G*, taste-bud; *C*, corium with injected blood-vessels; *M*, gland with duct.

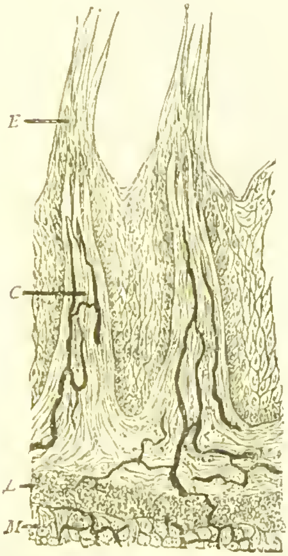

Fig. 394.—Section of two filiform papillæ, human. (Heitzmann.)

E, epithelium; *C*, corium; *L*, lymphoid tissue; *M*, muscular fibres of tongue.

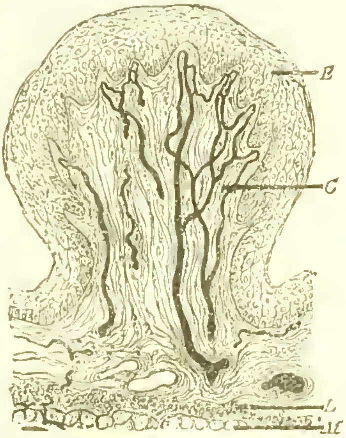

Fig. 395.—Section of fungiform papilla, human. (Heitzmann.) Letters as in previous figure.

and a few others elsewhere, yield an albuminous secretion (*serous glands, glands of Ebner*).

The mucous membrane at the back of the tongue contains a large amount of lymphoid tissue.

Taste-buds.—The minute gustatory organs which are known as *taste-buds* or taste-bulbs may be seen in sections which pass through the

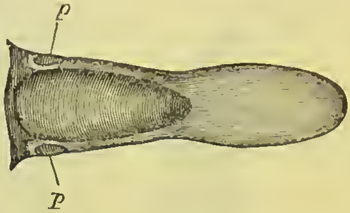

FIG. 396.—TONGUE OF RABBIT, SHOWING THE SITUATION OF THE PAPILLÆ FOLIATÆ, *p*.

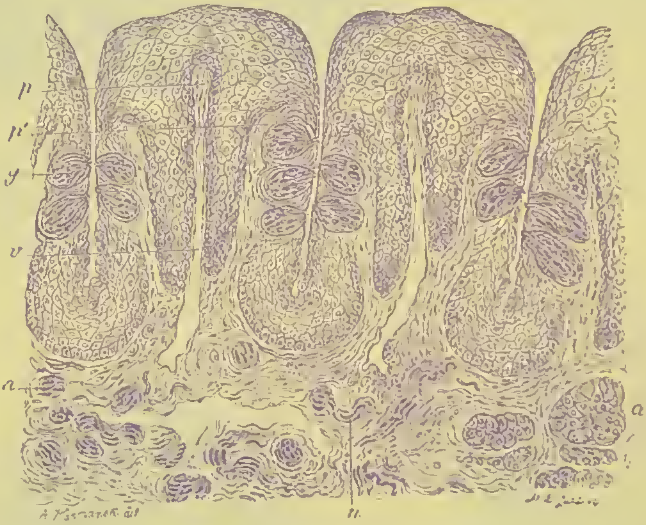

FIG. 397.—VERTICAL SECTION OF PAPILLA FOLIATA OF THE RABBIT, PASSING ACROSS THE FOLIÆ. (Ranvier.)

p, central lamina of the corium; *v*, section across a vein, which traverses the folium; *p′*, lateral lamina in which the nerve-fibres run; *g*, taste-bud; *n*, sections of nerve-bundles; *a*, serous gland.

papillæ vallatæ or the papillæ fungiformes; they are also present here and there in the epithelium of the general mucous membrane of the tongue, especially at the back and sides, and occur also upon the under surface of the soft palate, and on the epiglottis. But they are most easily studied in the papillæ foliatæ of the rabbit, two small oval areas lying on either side of the back of the tongue, and marked transversely with a number of small ridges or laminæ with intervening furrows (see fig. 396). Sections across the ridges show numerous taste-buds embedded in the thick epithelium which clothes their sides (fig. 397).

The taste-buds are ovoid clusters of epithelium-cells which lie in cavities in the stratified epithelium (fig. 398). The base of the taste-bud rests upon the corium of the mucous membrane, and receives a branch of the glosso-pharyngeal nerve; the apex is narrow and communicates with the cavity of the mouth by a small pore in the superficial epithelium (*gustatory pore*, fig. 398, *p*).

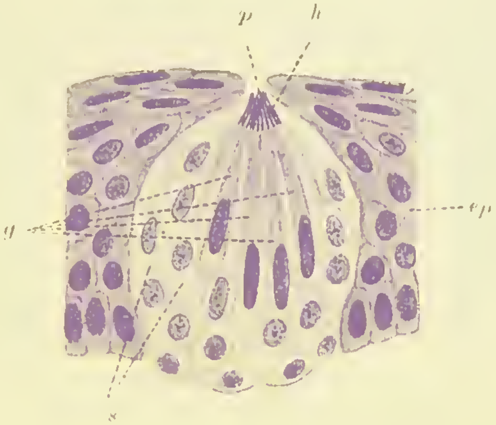

FIG. 398.—A TASTE-BUD WITHIN THE STRATIFIED EPITHELIUM OF THE TONGUE. (Sobotta.) ×500.

g, gustatory cells; *s*, sustentacular cells; *ep*, epithelium; *p*, gustatory pore; *h*, hairlets.

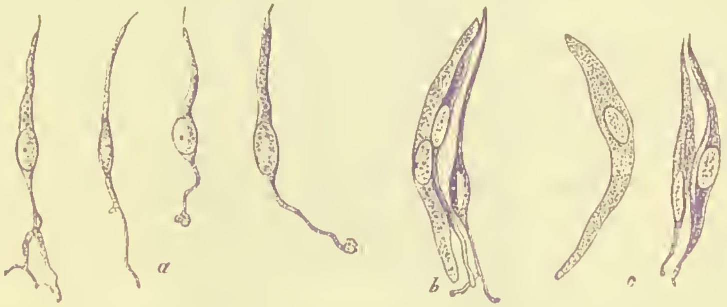

FIG. 399.—VARIOUS CELLS FROM TASTE-BUD OF RABBIT. (Engelmann.) 600 diameters.

a, four gustatory cells from central part; *b*, two sustentacular cells, and one gustatory cell, in connection; *c*, three sustentacular cells.

The cells which compose the taste-buds are of two kinds, viz.: 1. The *gustatory cells* (fig. 399, *a*), which are delicate fusiform or bipolar cells composed of the cell-body or nucleated enlargement, and of two processes, one distal, the other proximal. The distal process is nearly straight, and passes towards the apex of the taste-bud, where it terminates in a small, highly refracting cilium-like appendage, which projects into the gustatory pore above mentioned, but the cell-body does not itself quite reach the pore. The proximal process is more delicate than the other, and is often branched and varicose. The nerve-fibres (fig. 400) terminate in ramifications amongst the gustatory cells (Retzius). 2. The *sustentacular cells* (fig. 399, *c*), which are elongated cells, mostly flattened, and pointed at their ends; they lie between the gustatory cells, which they thus appear to support, and in addition they form a sort of envelope or covering to the taste-bud. Between the cells of the taste-bud lymph-corpuscles are often seen, having probably wandered hither from the subjacent mucous membrane. Connective-tissue fibrils penetrate between the taste-bud and the stratified epithelium in which it is embedded (Drasch).

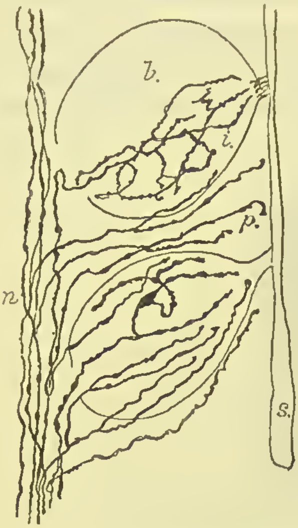

FIG. 400. — NERVE-ENDINGS IN TASTE-BUDS. (G. Retzius.) *n*, nerve-fibres; *b*, taste-buds in outline; *i*, ending of fibrils within taste-bud; *p*, ending in epithelium between taste-buds; *s*, sulcus into which the gustatory pores open.

The **mucous membrane of the mouth** is lined by a stratified epithelium (fig. 401) into which microscopic vascular and, in some parts, nerve-containing papillæ project. The corium is formed of connective tissue and contains within and beneath it a large number of small secretory glands (buccal glands). Most of these secrete mucus, but some are of the mixed type (see under salivary glands, p. 325): this is the case, for example, with the glands of the lips. The ducts of the buccal glands open everywhere upon the surface of the membrane, and the openings of the large ducts belonging to the salivary glands are also seen at certain parts.

The **pharynx** is composed of a *fibrous membrane* which is encircled by striated muscles, the *constrictors*, and lined by *mucous membrane*. The mucous membrane is covered on its inner surface over the upper part of the pharynx with ciliated epithelium, which is continuous with that of the nostrils, and through the Eustachian tube with that of the tympanum. Below the level of the soft palate the epithelium is stratified like that of the mouth and gullet, into which it passes. In certain parts the mucous membrane contains a large amount of lymphoid tissue, and there are numerous glands opening on its surface.

The **œsophagus** or gullet, which passes from the pharynx to the stomach, consists, like the pharynx, of a *fibrous covering*, a *muscular coat*, a lining *mucous membrane*, and intervening connective tissue

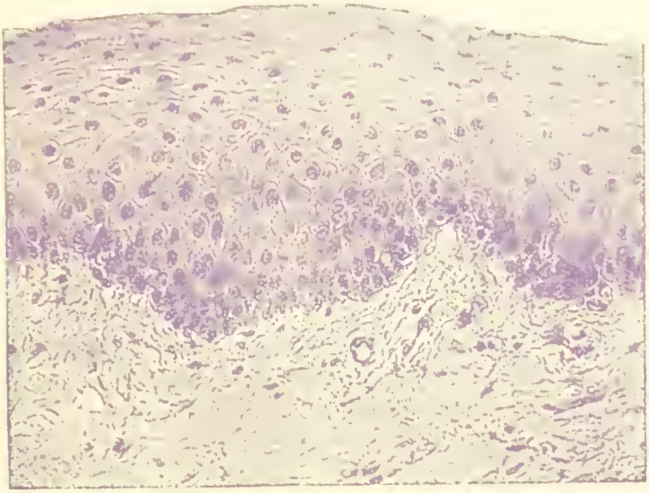

Fig. 401.—Section of the stratified epithelium of the fauces of the rabbit. Magnified 240 diameters.

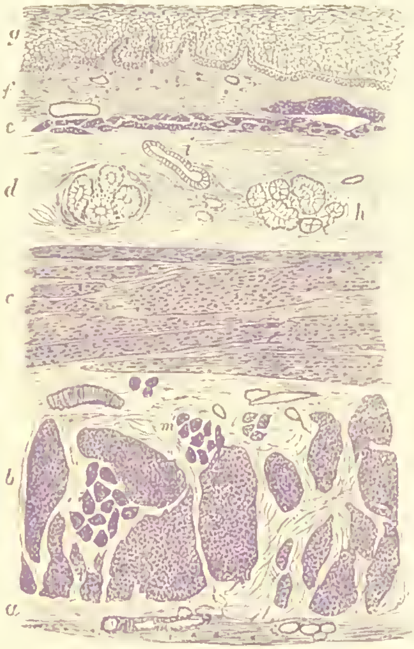

Fig. 402.—Section of the human œsophagus (Horsley.)

The section is transverse, and from near the middle of the gullet. *a*, fibrous covering; *b*, divided fibres of the longitudinal muscular coat; *c*, transverse muscular fibres; *d*, submucous or areolar layer; *e*, muscularis mucosæ; *f*, mucous membrane with papillæ; *g*, laminated epithelial lining; *h*, mucous gland; *i*, gland duct; *m'*, striated muscular fibres in section.

(*submucous* or *areolar coat*) (fig. 402). The muscular coat is much more regularly arranged than that of the pharynx, and is composed of striated muscle in about its upper third only, the rest being of the plain variety. There are two layers of the muscular coat—an outer layer, in which the fibres run longitudinally, and an inner, in which they have a circular arrangement. The mucous membrane is lined by a stratified epithelium, into which microscopic papillæ from the corium project. The corium is formed of an areolar tissue, and its limits are marked externally by a narrow layer of longitudinally disposed plain muscular fibres, the *muscularis mucosæ*. This is separated from the proper muscular coat by the areolar coat, which contains the larger branches of the blood-vessels and lymphatics, and also the mucous glands of the membrane. The ducts of these glands are large and usually pass through a nodule of lymphoid tissue, lymph-cells from which infiltrate the epithelium of the duct and may pass out into its lumen.

Besides these mucous glands, there are met with both at the upper or laryngeal part of the œsophagus and at the lower or cardiac end a certain number of small tubulo-racemose glands of a different character. They are confined to the mucous membrane, not penetrating the muscularis mucosæ, and their ducts open upon and not between the papilla of the mucous membrane. They closely resemble the cardiac glands of the stomach (see fig. 410, p. 329), and it is frequently found that the epithelium of the surface in the immediate neighbourhood of their ducts is similar to that lining the stomach.

There are two ganglionated nerve-plexuses, one in the muscular coat and one in the submucous coat, like those of the intestine (Klein).

LESSON XXX.

THE SALIVARY GLANDS.

1. Section of the submaxillary gland (dog). The gland may be hardened in alcohol or formol and stained with haematoxylin-eosin or with iron haematoxylin by Heidenhain's method. Notice the acini filled with clear (mucus-secreting) cells, the nuclei of which usually lie near the basement-membrane. Notice here and there, outside the clear cells, demilunes or crescents of small darkly stained granular-looking (albuminous) cells. Observe also the sections of the ducts with their striated columnar epithelium. If possible find a place where one of the ducts is passing into the alveoli. Sketch under a high power.

2. Study sections of the parotid and sublingual glands prepared in a similar way, and notice the differences between the three glands.

3. Examine small pieces of both submaxillary and parotid gland of the dog fresh in 2 per cent. salt solution. In the submaxillary gland notice that the alveolar cells are swollen out with large granules or droplets of mucigen, which swell up in water to form large clear vacuoles. Dilute acids and alkalies produce a similar change, but more rapidly. The cells of the parotid gland are also filled with granules, but they are smaller. The granules are also swollen up and dissolved by these fluids. Make a sketch from each preparation under a high power.

4. To study the changes which the alveolar cells undergo during secretion, pilocarpine is administered to an animal in sufficient amount to produce copious salivation; after half an hour the animal is killed and its salivary glands are examined as in preparation 3. The granules are not seen in preparations that have been in alcohol, but osmic acid preserves them moderately well; they are well seen in sections from picric hardened glands.

The **salivary glands** may be looked upon as typical of secreting glands in general. They are composed of a number of *lobules* bound together loosely by connective tissue. Each small lobule is formed of a group of irregularly saccular or tubular *alveoli* or *acini* from which a duct passes, and this, after uniting with other ducts, eventually leaves the gland to open upon the surface of the mucous membrane of the mouth.

The alveoli are inclosed by a basement-membrane, which has flattened branched cells on its inner surface, next to the epithelium (fig. 403). It may be shown by teasing the fresh gland substance in water (Langley). This basement-membrane is continued along the ducts. Within it is the epithelium, which in the alveoli is composed of polyhedral cells (fig. 404, *a*), but in the ducts is regularly columnar, except in that part of the duct which immediately opens into the alveoli (*junctional part*); in this it is flattened (*d'*). The columnar epithelium of the ducts is peculiar, in that the cells show a distinction into two unequal zones, an outer, larger, striated zone, and an inner smaller, granular one (fig. 404, *d*).

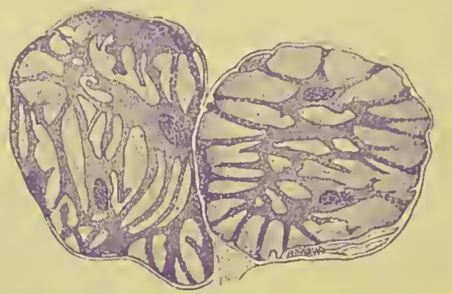

FIG. 403.—MEMBRANA PROPRIA OF TWO ALVEOLI. (v. Ebner) × 600.

The preparation is taken from a mucous gland of the rabbit.

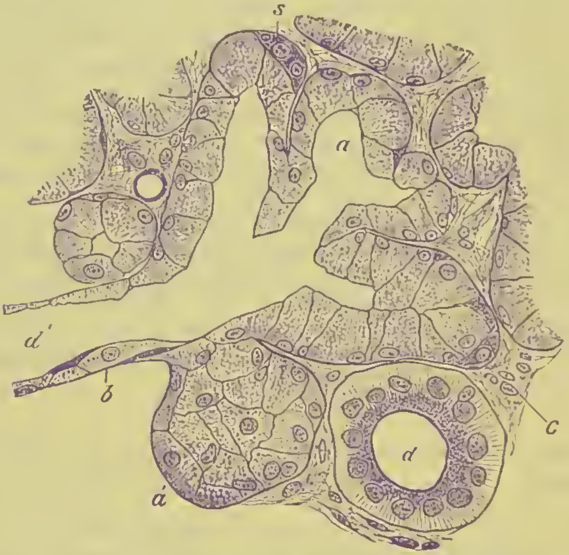

FIG. 404.—SECTION OF THE SUBMAXILLARY GLAND OF THE DOG, SHOWING THE COMMENCEMENT OF A DUCT IN THE ALVEOLI. Magnified 425 diameters.

a, one of the alveoli, several of which are in the section shown grouped around the commencement of the duct, *d'*; *a'*, an alveolus, not opened by the section; *b*, basement-membrane in section; *c*, interstitial connective tissue of the gland; *d*, section of a duct which has passed away from the alveoli, and is now lined with characteristically striated columnar cells; *s*, semilunar group of darkly stained cells at the periphery of an alveolus.

The cells of the alveoli differ according to the substance they secrete. In alveoli which secrete mucus, such as all the alveoli of the dog's submaxillary (fig. 404), and some of the alveoli of the same gland in man (fig. 107), the cells, if examined in normal saline solution or after hardening with alcohol, are clear and swollen. But if examined rapidly in serum, or in solutions of salt of from 2 to 5 per cent., they are often seen to be occupied by large and distinct granules (Langley). These granules can also be rendered visible by certain methods of staining, when it is apparent that they are not present as such in all the cells, but have in many cells become clear and swollen, and converted into a substance which is known as *mucigen* (fig. 409, *a*). Similar granules are seen also in the cells lining the gland ducts; here also they are found to vary in size and number with the condition of activity of the gland (fig. 411). The mucigen is dissolved out of the cell and discharged as *mucus* into the lumen of the alveolus and into the ducts, when the gland is stimulated to activity. The cells

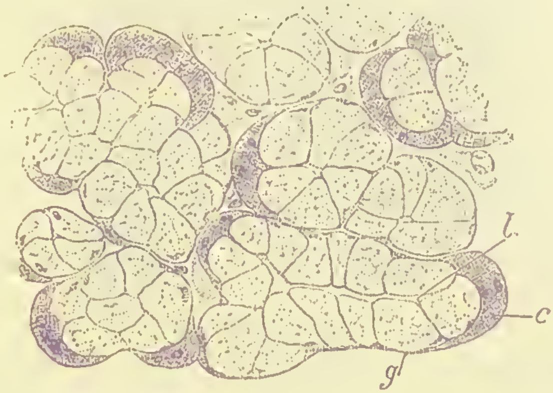

FIG. 405.—SECTION OF A DOG'S SUBMAXILLARY, AFTER A PROLONGED PERIOD OF REST. (Ranvier.)

l, lumen of alveolus; *g*, mucus-secreting cells; *c*, crescent, formed of albuminous cells.

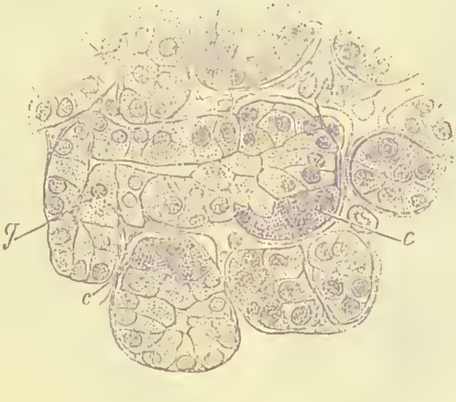

FIG. 406.—SUBMAXILLARY OF DOG, AFTER A PERIOD OF ACTIVITY. (Ranvier.)

The mucus-secreting cells, *g*, have discharged their secretion, and are smaller and stain better; the albuminous cells of the crescents, *c*, are enlarged.

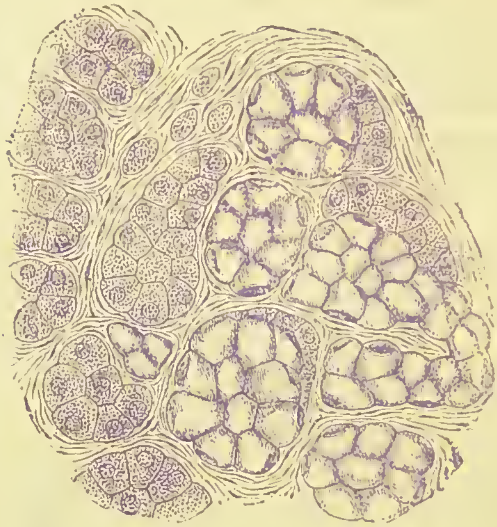

FIG. 407.—SECTION OF PART OF THE HUMAN SUBMAXILLARY GLAND. (Heidenhain.)

To the right of the figure is a group of mucous alveoli ; to the left a group of serous alveoli.

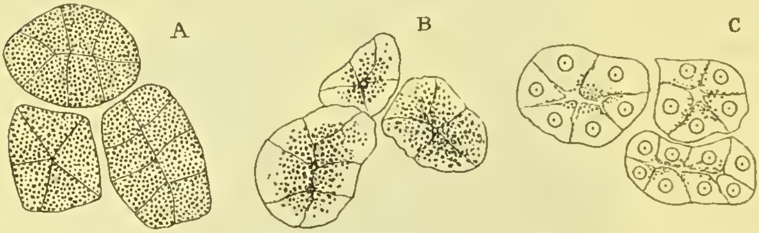

FIG. 408.—ALVEOLI OF A SEROUS GLAND. A, AT REST. B, AFTER A SHORT PERIOD OF ACTIVITY. C, AFTER A PROLONGED PERIOD OF ACTIVITY. (Langley.)

In A and B the nuclei are obscured by the granules of zymogen.

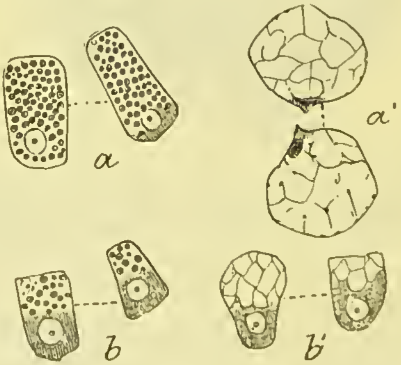

FIG. 409.—MUCOUS CELLS FROM FRESH SUBMAXILLARY GLANDS OF THE DOG. (Langley.)

a, from a resting or loaded gland ; *b*, from a gland which has been secreting for some time ; *a'*, *b'*, similar cells which have been treated with dilute acid.

are known as *mucous cells.* But in most alveoli there are some cells which do not contain mucigen, but small albuminous granules, and these often form crescentic groups which lie next to the basement-membrane (figs. 404, *s*, 405, *c*). These are the so-called *crescents of Gianuzzi;* their constituent cells are known also as *marginal* or *serous cells.* Special diverticula pass from the lumen of the alveoli between the mucous cells to penetrate to the crescents and to branch amongst and within their constituent cells; these diverticula are best shown by the Golgi method of staining (figs. 412, 413). They also occur in the purely *serous alveoli* (fig. 410), in which none of the cells secrete mucus, but watery or albuminous saliva. In these when the gland has been long

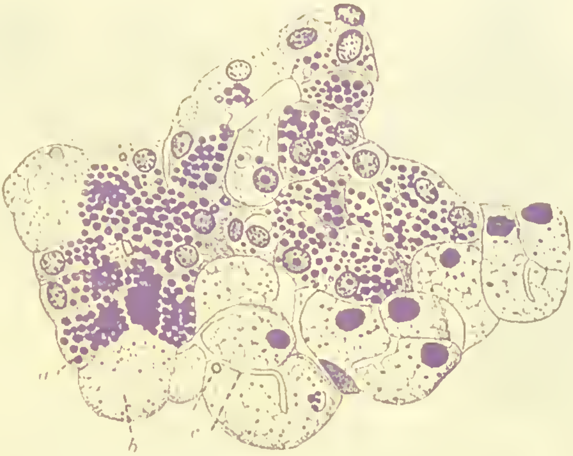

FIG. 410.—SUBMAXILLARY GLAND OF RABBIT. (E. Müller.)

The cells, which are all serous, are in different functional states, as indicated by the condition and staining of the granules. *a*, cell filled with darkly staining granules; *b*, clear cell; *c*, secretory canaliculi penetrating into the cells.

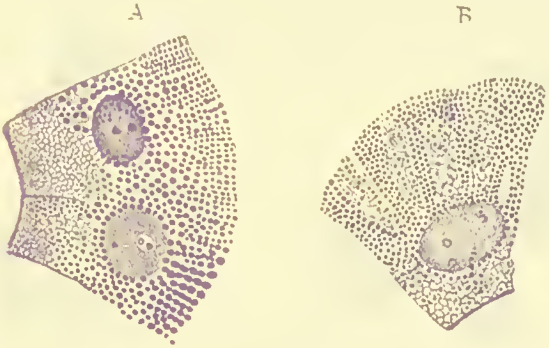

FIG. 411.—CELLS FROM DUCT OF PAROTID.

A, prior to secretion; B, after secretion (Mislawski and Smirnow).

at rest the cells are filled with granules, which do not swell with water nor form mucin; they appear to be albuminous in nature, and probably yield to the secretion of the gland its ferment (ptyalin) and its

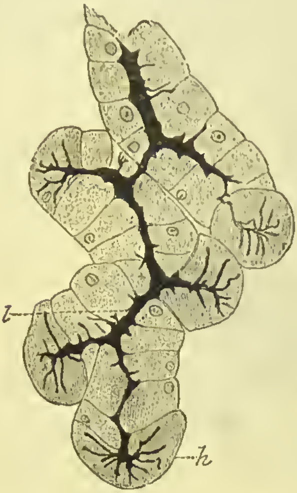

Fig. 412.—Alveoli of human sublingual gland prepared by Golgi method. (E. Müller.)

l, lumen stained, with lateral diverticula passing between mucus-secreting cells; *h*, longer diverticula penetrating into the "crescent" cells.

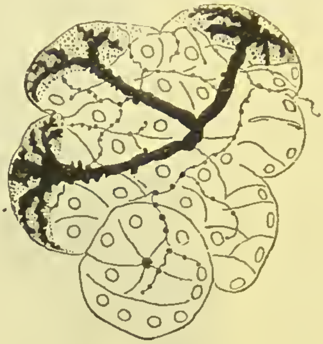

Fig. 413.—Alveoli of the submaxillary gland of the dog. (G. Retzius.) Golgi method.

The extensions of the lumen into the crescents of Gianuzzi are shown, and also the endings of nerve-fibrils.

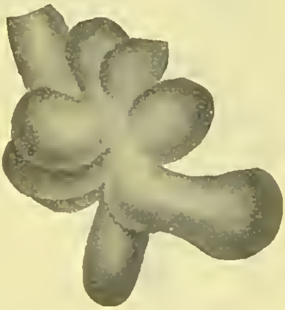

Fig. 414.—Alveoli from mucous portion of the human submaxillary gland, partly unravelled. (Peiser.)

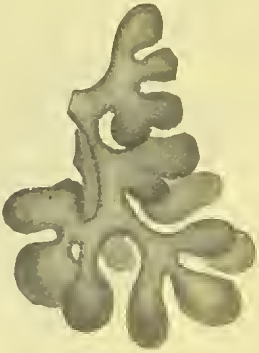

Fig. 415.—Alveoli from serous portion of the human submaxillary gland, partly unravelled. (Peiser.)

albumin. The granular substance within the cell is not the ferment, but the ferment is formed from it when the secretion is poured out. Hence it has been termed *zymogen* (mother of ferment). As Langley showed, the outer part of each cell becomes clear and free from granules after secretion (fig. 408).

In nearly all animals the parotid glands are composed of purely serous alveoli ; in man and most animals the submaxillary and sublingual glands have both serous and mucous alveoli or "mixed" alveoli, *i.e.*, alveoli containing both serous and mucous cells. The detached anterior parts of the sublingual gland, which in man are comparatively small, have purely mucous alveoli.

When the glands are unravelled and examined with the microscope it is found that the mucous and serous alveoli are somewhat different in shape, the mucous alveoli being larger, more uniform in shape, and linked on to the ducts by shorter and wider intermediate or junctional portions (compare fig. 414, which is from a mucous part of the human submaxillary, with fig. 415 from the serous part).

The largest ducts have a wall of connective tissue outside the basement-membrane, and also a few plain muscle cells. The blood-vessels of the salivary gland form a capillary network around each alveolus. The lymphatics commence in the form of lacunar vessels between the alveoli. Lymphoid nodules are occasionally found in the interstitial connective tissue. The nerve-fibres, which are derived both from the cerebro-spinal nerves and from the sympathetic, pass through ganglia before proceeding to their distribution. They ramify as fine varicose fibres amongst the alveolar cells (fig. 413); many are distributed to the blood-vessels.

The salivary glands are developed as buds from the epithelium of the buccal cavity, at first solid but becoming gradually hollowed out. To begin with they are simple, but undergo ramification as they grow into the mucous membrane and submucous tissue.

LESSON XXXI.

THE STOMACH.

1. Vertical longitudinal sections through the cardia, including the lower end of the œsophagus and the adjacent cardiac portion of the stomach. These are intended to show the abrupt transition of the stratified epithelium of the œsophagus into the columnar epithelium of the stomach, and also the character of the gastric and œsophageal glands in the immediate neighbourhood of the cardia. The sections may be stained with hæmatoxylin and eosin.

2. Sections of the fundus of the stomach cut perpendicularly to the surface of the mucous membrane.

In these sections the general arrangement of the coats of the stomach is to be studied. Sketches are to be made under a low power illustrating this arrangement, and others under a high power showing the structure of the glands of the mucous membrane.

Measure the whole thickness of the mucous membrane, the thickness of the muscular coat, the size of the columnar epithelium-cells of the surface, and that of the cells in the deeper parts of the glands.

3. Sections of the mucous membrane of the fundus, cut parallel to the surface.

These sections will show better than the others the arrangement of the cells in the glands.

4. Vertical sections of the mucous membrane from the pyloric region of the stomach. If the section is taken longitudinally through the pylorus, the transition of the gastric glands into the glands of Brunner of the duodenum will be made manifest. Make a sketch under a low power of one of the glands in its whole length, filling up some of the details with the high power.

5. Study the arrangement of the blood-vessels in vertical sections of the wall of a stomach the vessels of which have been injected.

The wall of the **stomach** consists of four coats, which, enumerated from without in, are as follows, viz.: *serous*, *muscular*, *areolar*, or *submucous*, and *mucous membrane* (fig. 416).

The *serous coat* is a layer which is derived from the peritoneum. It is deficient only along the lines of the lesser and greater curvatures.

The *muscular coat* consists of three layers of plain muscular fibres. Of these the bundles of the outer layer run longitudinally, those of the middle layer circularly, and those of the inner layer obliquely. The longitudinal and circular bundles become thicker and stronger towards the pylorus; at the pylorus itself the circular layer is greatly thickened to form a sphincter muscle. The oblique fibres are only present over the fundus.

The *areolar* or *submucous coat* is a layer of areolar tissue, which serves to unite the mucous membrane loosely to the muscular coat; in it ramify the larger branches of the blood-vessels and lymphatics.

The *mucous membrane* is a soft thick layer, generally somewhat corrugated in the empty condition of the organ. Its inner surface is covered by columnar-shaped epithelium-cells, all of which secrete mucus. They are prolonged into the ducts of the glands, but when these divide to form the tubules the cells become cubical, and lose their mucus-secreting character. Where the œsophagus passes into the stomach the stratified epithelium which lines the gullet gives place abruptly to the columnar epithelium of the stomach (fig. 417).

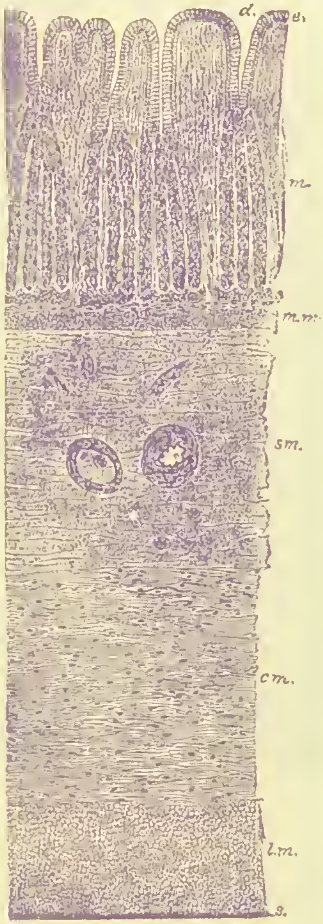

FIG. 416.—DIAGRAM OF SECTION THROUGH THE COATS OF THE STOMACH. (Mall.)

m, mucous membrane; *e*, epithelium; *d*, orifice of gland-duct; *m.m.*, muscularis mucosæ; *sm.*, submucosa; *c.m.*, circular muscular layer; *l.m.*, longitudinal muscular layer; *s*, serous coat.

In some animals the stratified epithelium of the œsophagus is continued over a more or less extensive tract of the gastric mucous membrane, but it always ends by a sharply defined line.

The thickness of the gastric mucous membrane is due to the fact that it is largely made up of long tubular glands, which open upon the inner surface. Between the glands the mucous membrane is formed of retiform with some lymphoid tissue. Externally the mucous membrane is bounded by the *muscularis mucosæ*, which consists of an external longitudinal and an inner circular layer of plain muscular fibres.

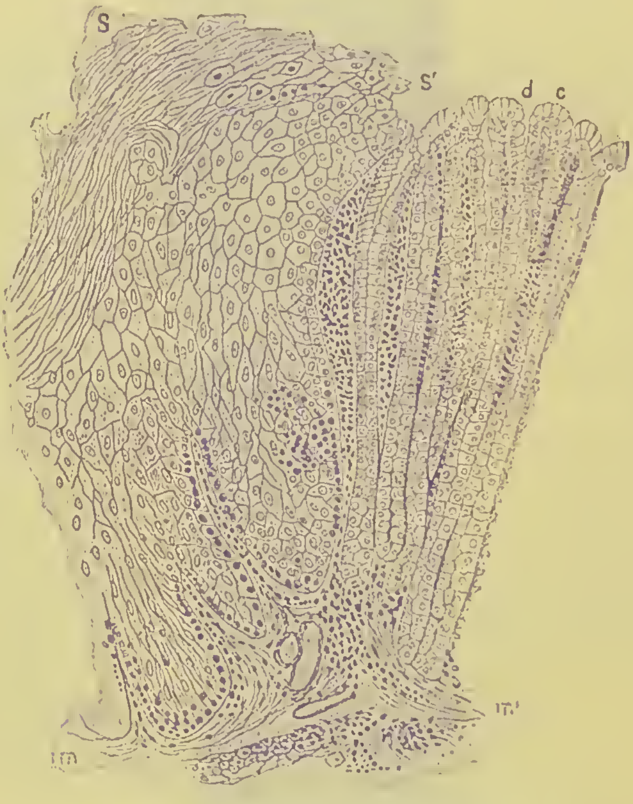

FIG. 417.—SECTION OF THE JUNCTION OF THE ŒSOPHAGEAL AND GASTRIC MUCOUS MEMBRANE OF THE KANGAROO. 135 diameters.

S, stratified epithelium of œsophagus abruptly discontinued at *S'* : *c*, columnar epithelium of gastric mucous membrane ; *d*, orifices or ducts of glands of the cardia ; *m*, corium of œsophageal mucous membrane sending papillæ into the epithelium ; *m'*, corium of gastric mucous membrane.

Gastric glands.—These are formed of a basement-membrane lined with epithelium. Each gland consists of *secreting tubules*, from one to four in number, opening at the surface into a larger tube, the *duct* of the gland. The duct is in all cases lined by mucus-secreting epithelium of the same character as that which covers the inner surface of the mucous membrane, but the epithelium of the secreting tubules is different from this, and also differs somewhat in the glands of different regions of the organ. The following varieties of gastric glands are met with:

(1) *Glands of the cardia.*—These are found in man close to the œsophageal opening or cardia; they are of two kinds: (*a*) simple tubules, very similar to the crypts of Lieberkühn of the intestine and (*b*) small tubulo-racemose glands (fig. 418). The latter are commonest in man: the former may occur in considerable number in some animals (fig. 417). The secreting tubules of the racemose glands are lined by cells which are granular in appearance and of a short columnar form, and of the same nature throughout the length of the tubule, except near the orifice (duct), where they give place to columnar mucus-secreting cells. Bensley describes some of the tubules as lined with mucus-secreting cells throughout. Occasionally one or two oxyntic cells may be present in the tubules.

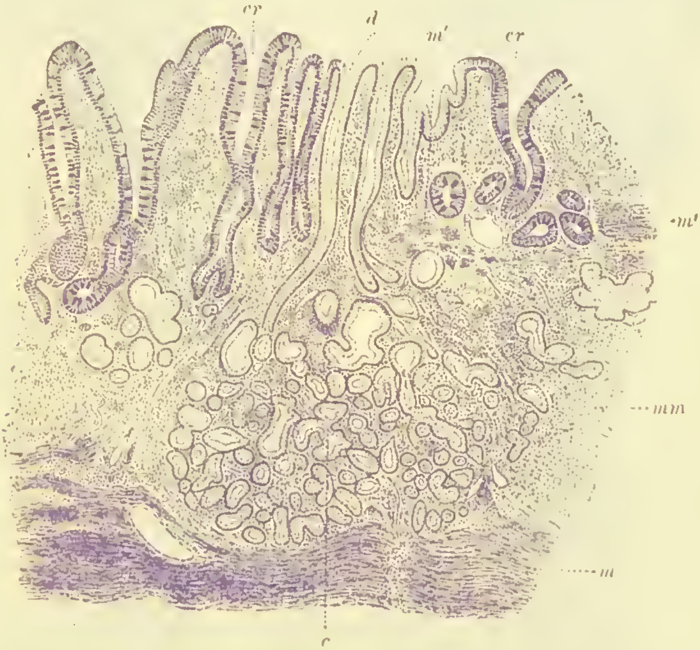

FIG. 418.—SECTION OF HUMAN STOMACH NEAR THE CARDIA. (v. Ebner, after J. Schaffer.) × 45.

c, cardiac glands; *d*, their ducts; *cr*, glands similar to crypts of Lieberkühn, with goblet cells; *mm*, mucous membrane; *m*, muscularis mucosæ; *m'*, muscular tissue within mucous membrane.

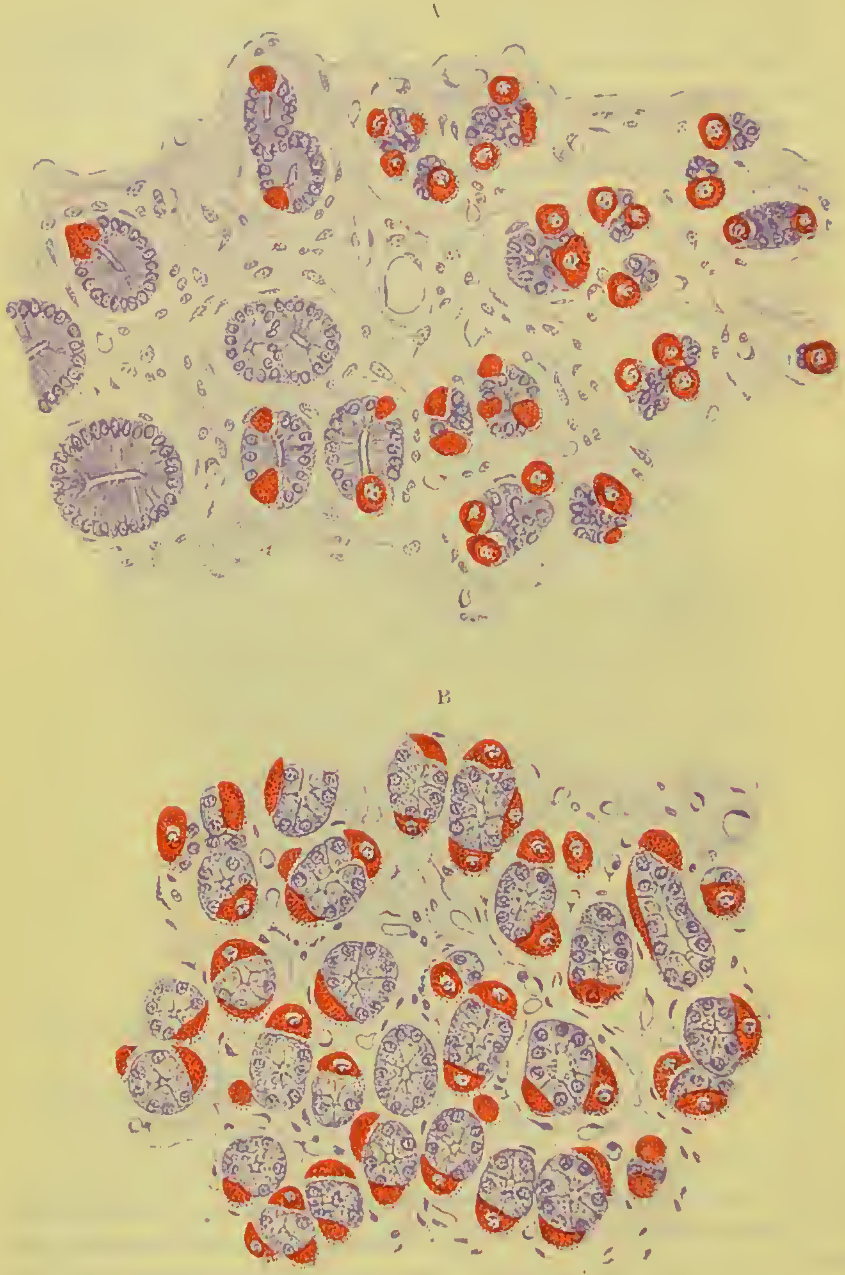

FIG. 419.—SECTIONS OF THE MUCOUS MEMBRANE OF THE FUNDUS OF THE DOG'S STOMACH PASSING ACROSS THE LONG AXIS OF THE GLANDS.

A, Section close to but not quite parallel with the surface, and including on the left the gland ducts and on the right the commencing gland tubules. Notice the oxyntic cells beginning to appear between the columnar cells of the ducts.

B, Deeper part of the same section, showing the lumina of the gland tubules surrounded by chief cells, with the oxyntic cells altogether outside them.

Glands of a somewhat similar character occur near the lower end of the œsophagus. Generally at the place where their ducts open the œsophageal epithelium becomes columnar instead of stratified.

(2) *Glands of the fundus* (*oxyntic glands*) (figs. 419, 420, 421, 422).—In these glands the tubules are usually relatively long and the duct short. The epithelium of the tubules is composed of two kinds of cells. Those of the one kind, which form a continuous lining to the tubule, are somewhat polyhedral in shape, and in stained sections look clearer and smaller than the others, but in the fresh glands, and with certain methods of staining, it can be seen that they are partly filled with granules (fig. 420). The granules are most numerous in the inner portion of the cell, an outer zone being left clear. After prolonged activity this outer zone increases in size while the granules

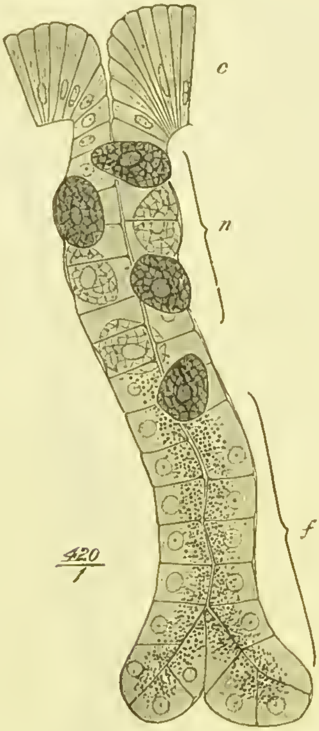

Fig. 420.

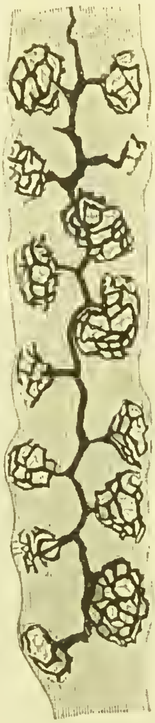

Fig. 421.

Fig. 420.—A fundus gland of simple form from the bat's stomach. Osmic acid preparation. (Langley.)

c, columnar epithelium of the surface; *n*, neck of the gland with central and parietal cells; *f*, base, occupied only by principal or central cells, which exhibit the granules accumulated towards the lumen of the gland.

Fig. 421.—A fundus gland prepared by Golgi's method, showing the mode of communication of the parietal cells with the gland-lumen. (E. Müller.)

diminish in number, as in the analogous cases of the pancreas and parotid glands (Langley). The cells are believed to form pepsin, and are termed the *chief cells* of the cardiac glands, or from their relative position in the tubule immediately surrounding the lumen, the *central cells.* Scattered along the tubule, and lying between the chief cells

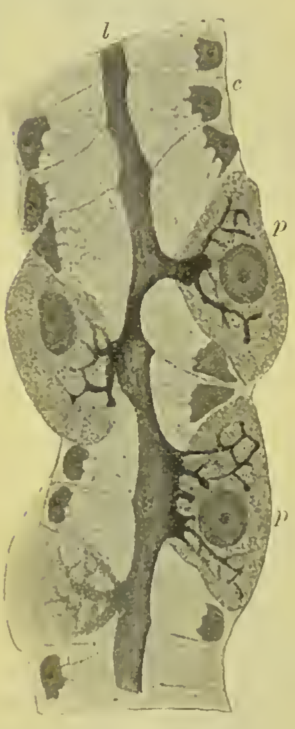

FIG. 422.

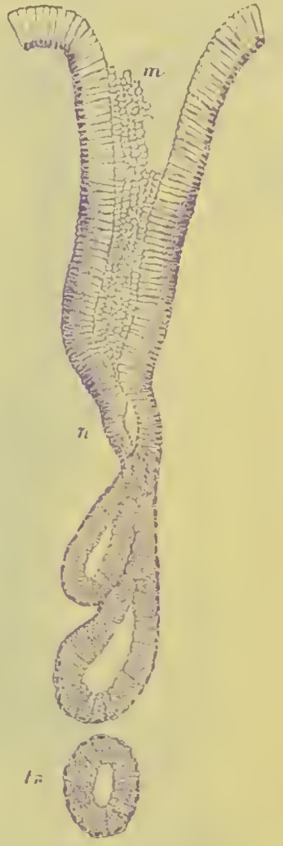

FIG. 423.

FIG. 422.—PART OF TUBULE OF A FUNDUS GLAND, WITH THE LUMEN AND SECRETORY CANALICULI STAINED; THE GLAND CELLS ARE ALSO SHOWN. (Zimmermann.)

c, chief or central cells; *p*, parietal or oxyntic cells; *l*, lumen of tubule prolonged into arborescent canaliculi which penetrate to the parietal cells.

FIG. 423.—A PYLORIC GLAND, FROM A SECTION OF THE DOG'S STOMACH. (Ebstein.)

m, mouth; *n*, neck; *tr*, a deep portion of a tubule cut transversely.

and the basement-membrane, are a number of large spheroidal or ovoidal cells. These are the *parietal* or *oxyntic cells.*[1] Each parietal cell is surrounded and penetrated by a network of minute passages, communicating with the lumen of the gland by a fine canal, which passes between the central cells (figs. 421, 422); but in the neck of the gland the parietal cells abut against the lumen, being here wedged in between the mucus-secreting cells (fig. 419, A).

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[1] So called because they are believed to produce the acid of the gastric secretion.

(3) *Glands of the pyloric canal* (fig. 423).—In the glands of the pyloric canal the *ducts* are much longer than in those of the fundus, and the secreting tubules possess cells of only one kind.[1] These correspond to the chief cells of the fundus glands, but are not quite identical with them in appearance, the granules being much less distinct. The cells are of a columnar or cubical shape, and in the fresh condition of a granular appearance; quite unlike the clear columnar epithelium of the surface, which is formed, as elsewhere, of long tapering cells, the outer part of which is filled with mucigen.

At the pylorus itself the gastric glands become considerably lengthened and enlarged, and are continued into the submucous tissue, the muscularis mucosæ being here deficient; they thus present transitions to the glands of Brunner, which lie in the submucous tissue of the duodenum (fig. 424).

Scattered amongst the ordinary secreting cells of the pyloric glands, cells are seen here and there which stain differently from the rest, and probably have a different function (Stöhr). Occasionally oxyntic cells are met with in the pyloric glands and even in Brunner's glands in the duodenum (Kaufmann).

The *blood-vessels* of the stomach are very numerous, and pass to the organ along its curvatures. The arteries traverse the muscular coat, giving off branches to the capillary network of the muscular tissue, and ramify in the areolar coat. From this, small tortuous arteries pierce the muscularis mucosæ, and break up into capillaries near the bases of the glands (fig. 425). The capillary network extends between the glands to the surface, close to which it terminates in a plexus of relatively large venous capillaries which encircle the mouths of the glands. From this plexus straight venous radicles pass through the mucous membrane, pierce the muscularis mucosæ, and join a plexus of veins in the submucous tissue. From these veins blood is carried away from the stomach by efferent veins, which accompany the entering arteries.

The *lymphatics* (fig. 426) arise in the mucous membrane by a plexus of large vessels dilated at intervals, and looking in sections like clefts in the interglandular tissue. From this plexus the lymph is carried into large valved vessels in the submucous coat, and from these, efferent vessels run through the muscular coat to reach the serous

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[1] In man it is only quite near the pyloris that parietal cells are altogether absent.

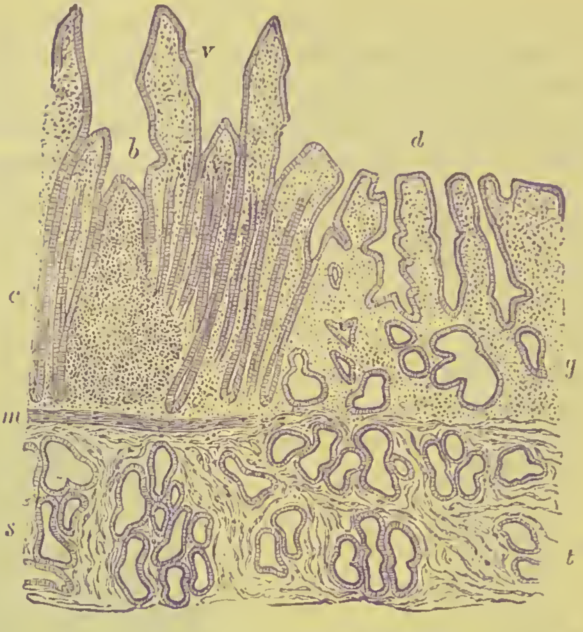

FIG. 424.—SECTION THROUGH THE PYLORUS, INCLUDING THE COMMENCEMENT OF THE DUODENUM. (Klein.)

v, villi of duodenum; *b*, apex of a lymphoid nodule; *c*, crypts of Lieberkühn; *s*, secreting tubules of Brunner's glands; *d*, ducts of pyloric glands of the stomach; *g*, tubes of these glands in mucous membrane; *t*, deeper lying tubes in submucosa, corresponding to secreting tubules of Brunner's glands of duodenum; *m*, muscularis mucosæ.

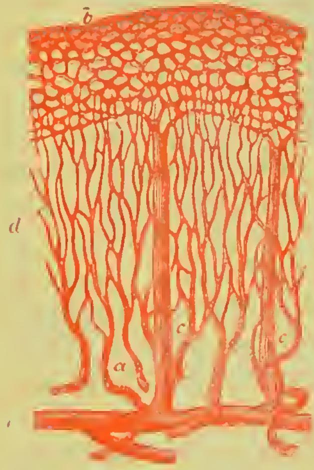

FIG. 425.—PLAN OF THE BLOOD-VESSELS OF THE STOMACH. (Modified from Brinton.)

a, small arteries passing to break up into the fine capillary network, *d*, between the glands; *b*, coarser capillary network around the mouths of the glands; *c*, *c*, veins passing vertically downwards from the superficial network; *e*, larger vessels in the submucosa.

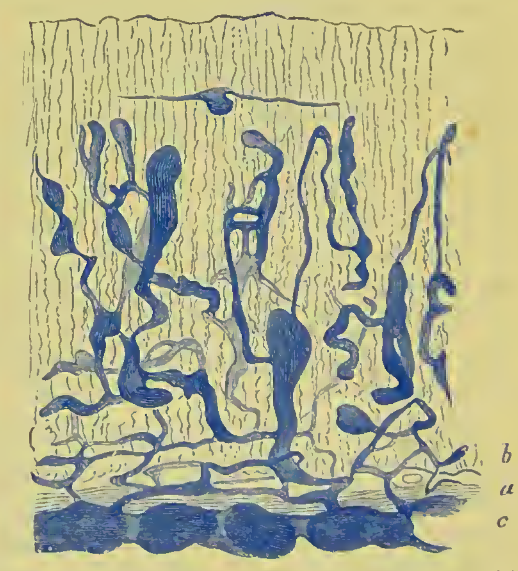

FIG. 426.—LYMPHATICS OF THE HUMAN GASTRIC MUCOUS MEMBRANE, INJECTED. (C. Lovèn.)

The tubules are only faintly indicated; *a*, muscularis mucosæ; *b*, plexus of fine vessels at base of glands; *c*, plexus of larger valved lymphatics in submucosa.

membrane, underneath which they pass away from the organ. The muscular coat has its own network of lymphatic vessels. These lie between the two principal layers, and their lymph is poured into the efferent lymphatics of the organ.

The nerves have the same general arrangement and mode of distribution as those of the intestine (see next Lesson).

LESSONS XXXII. AND XXXIII.

THE SMALL AND LARGE INTESTINE.

1. SECTIONS of the duodenum, jejunum, and ileum, vertical to the surface. The three parts of the intestine may be embedded in the same paraffin block, and the sections stained and mounted together. Choose a part of the ileum which includes a Peyer's patch. Observe the nodules of lymphoid tissue which constitute the patch and which extend into the submucous tissue. Observe the lymphoid cells in the superjacent epithelium. Notice also the sinus-like lymphatic or lacteal vessel which encircles the base of each nodule. In the duodenum study the glands of Brunner in the submucous tissue. Make a general sketch of each section under a low power and draw a villus under the high power. The general arrangement and structure of the intestinal wall is to be studied in these sections.

2. Sections parallel to the surface of the intestine, and therefore across the long axis of the villi and glands of the mucous membrane. In order to keep the sections of the villi together so that they are not lost in the mounting, it is necessary either to embed in celloidin or, if paraffin be used, to employ an adhesive method of mounting.

In this preparation, sketch the transverse section of a villus and of some of the crypts of Lieberkühn.

3. To study the process of fat-absorption, kill a frog two or three days after feeding with bacon fat. Put a very small shred of the mucous membrane of the intestine into osmic acid (0·5 per cent.) and another piece into a mixture of 2 parts Müller's fluid and 1 part osmic acid solution (1 per cent.). After forty-eight hours teased preparations may be made from the osmic acid preparation, in the same manner as directed in Lesson VIII., § 1. The piece in Müller and osmic acid may be left for ten days or more in the fluid. When hardened, sections are made by the freezing method and mounted in glycerine. They may also be cut from paraffin and mounted in dammar.

4. Sections of small intestine the blood-vessels of which have been injected. Notice the arrangement of the vessels in the several layers. Sketch carefully the vascular network of the villus.

5. From a piece of intestine which has been stained with chloride of gold tear off broad strips of the longitudinal muscular coat, and mount them in glycerine. It will generally be found that portions of the nervous plexus of Auerbach remain adherent to the strips, and the plexus can in this way easily be studied.

From the remainder of the piece of intestine tear off with forceps the fibres of the circular muscular layer on the one side, and the mucous membrane on the other side, so as to leave only the submucous tissue and the muscularis mucosæ. This tissue is also to be mounted flat in glycerine; it contains the plexus of Meissner.

Sketch a small portion of each plexus under a high power. The plexuses can also be studied by the methylene-blue and reduced silver methods (see Appendix).

6. Sections of the large intestine, perpendicular to the surface. These will

show the general structure and arrangement of the coats. Sketch under a low power.

7. Sections of the mucous membrane of the large intestine parallel to the surface, and therefore across the glands. Sketch some of the glands and the interglandular tissue under a high power.

8. The arrangement of the blood-vessels of the large intestine may be studied in sections of the injected organs.

The wall of the **small intestine** consists, like that of the stomach, of four coats (fig. 427).

The *serous coat* is complete except over part of the duodenum.

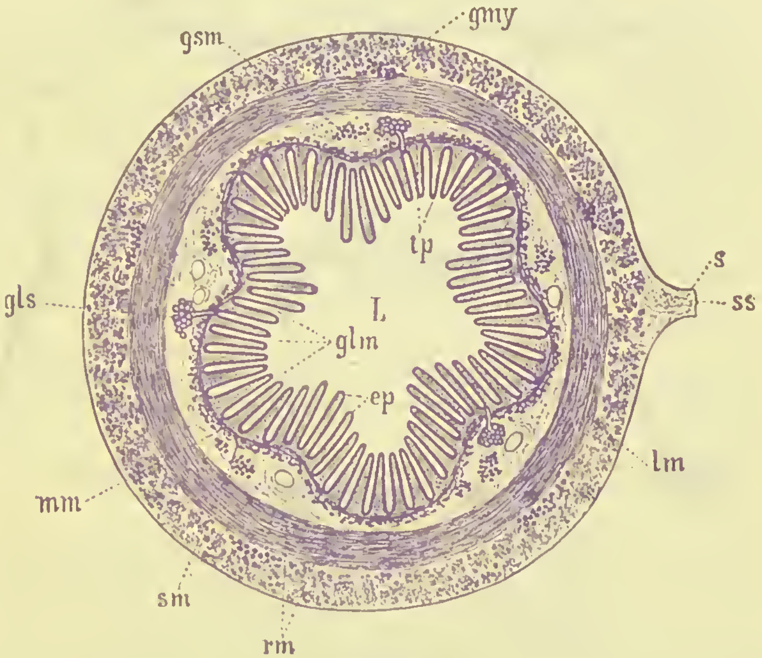

FIG. 427.—DIAGRAM OF SECTION OF ALIMENTARY TUBE. (Sobotta.)

L, lumen; *glm*, glands of mucous membrane; *ep*, epithelium; *gls*, glands in submucosa; *mm*, muscularis mucosæ; *sm*, submucous coat; *rm*, circular muscular layer; *lm*, longitudinal muscular layer; *s*, serous coat; *ss*, mesentery; *gmy*, ganglion of plexus myentericus; *gsm*, ganglion of plexus submucosus,

The *muscular coat* is composed of two layers of muscular tissue, an outer longitudinal and an inner circular. Between them lies a network of lymphatic vessels, and also the close gangliated plexus of non-medullated nerve-fibres known as the *plexus myentericus* of Auerbach. The ganglia of this plexus may usually be seen in vertical sections of the intestinal wall (in figs. 432, 435), but the plexus, like the one in the submucous coat immediately to be described, can only be properly displayed in preparations made with chloride of gold (fig. 428) or methylene blue or by a silver method.

The *submucous coat* is like that of the stomach; in it the blood-vessels and lacteals ramify before entering or after leaving the mucous membrane, and it contains a gangliated plexus of nerve-fibres—the *plexus of Meissner*—which is finer than that of Auerbach and has fewer ganglion cells (fig. 429). Its branches are chiefly supplied to the muscular fibres of the mucous membrane, but also to the glands and villi (fig. 430).

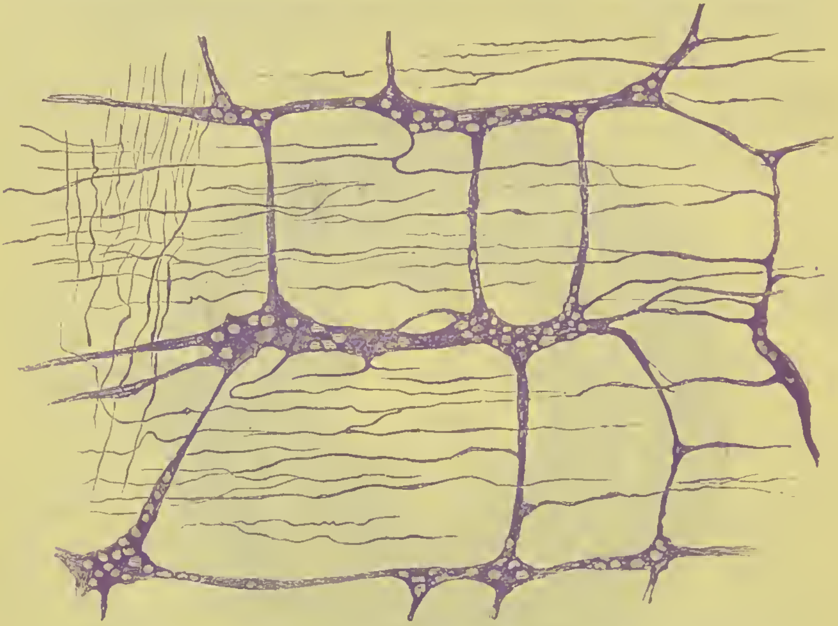

FIG. 428.—AUERBACH'S PLEXUS, FROM THE MUSCULAR COAT OF THE INTESTINE. (Cadiat.)

These enteric gangliated plexuses contain two kinds of nerve-cell (fig. 431). One kind has a number of much branched dendrons easily distinguishable from the axon; the other kind is characterised by the presence of a number of processes hardly distinguishable from one another. This last type of cell is the only one found in Meissner's plexus.

The *mucous membrane* is bounded next to the submucous coat by a double layer of plain muscular fibres (*muscularis mucosæ*). Bundles from this pass inwards through the membrane towards the inner surface and penetrate also into the villi. The mucous membrane proper is pervaded with simple tubular glands—the *crypts of Lieberkühn* (figs. 432, 433, 435)—which are lined throughout by a columnar epithelium, with scattered goblet cells, like that which covers the

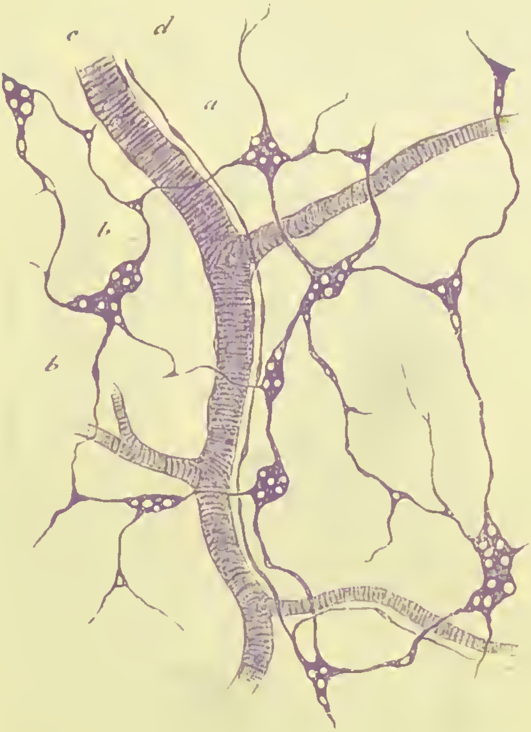

FIG. 429.—MEISSNER'S PLEXUS FROM THE SUBMUCOUS COAT. (Cadiat.)
a, ganglion; *b*, *b*, nervous cords; *c*, a blood-vessel; *d*, an entering sympathetic nerve.

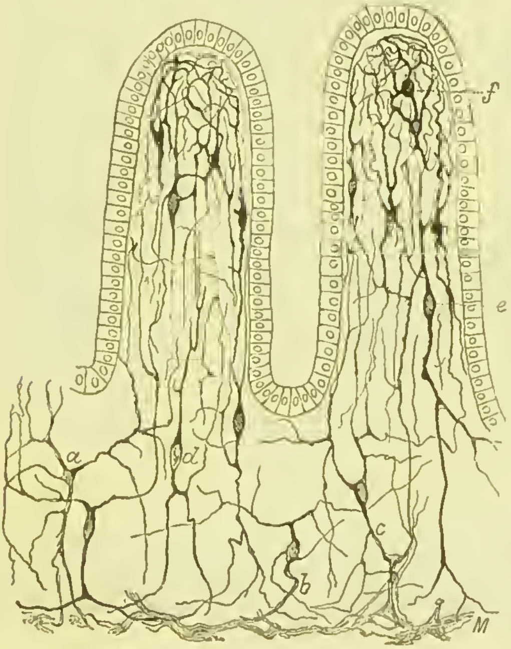

FIG. 430. NERVES OF THE MUCOUS MEMBRANE OF THE SMALL INTESTINE. (Cajal.)
M, part of Meissner's plexus; *a-f*, small nerve-cells and nerve-fibres in the tissue of the mucous membrane and villi.

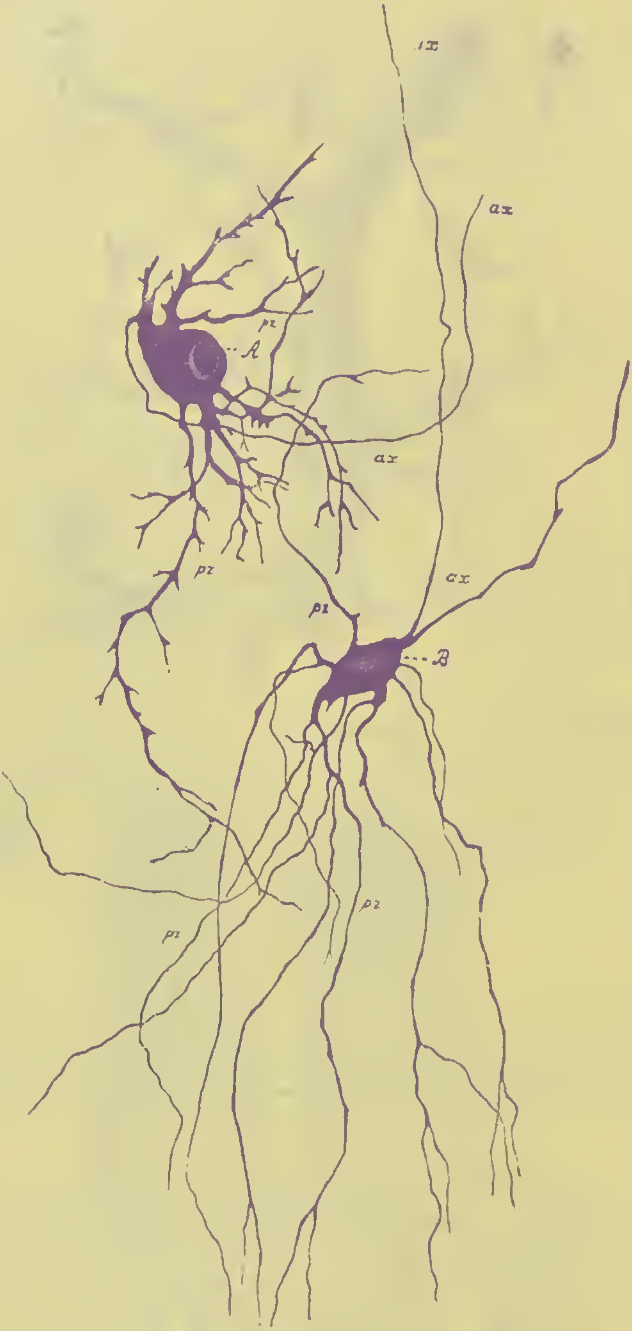

FIG. 431.—TYPICAL NERVE-CELLS FROM ENTERIC GANGLIA. (Dogiel.)
A, a cell with numerous minute ramified dendrons; *B*, a cell with numerous almost unbranched axon-like dendrons; *ax*, axons; *pz*, dendrons.

general surface and the villi. At the fundus of each crypt are a few cells containing well-marked granules (Paneth). The cells of the glands show frequent mitoses; it is stated that the epithelium of the general surface becomes regenerated from them (Bizzozero). The mucous membrane between these glands is mainly composed of reticular tissue, which contains here and there nodules of lymphoid tissue. These nodules constitute when they occur singly the so-called *solitary glands* of the intestine (fig. 434), and when aggregated together

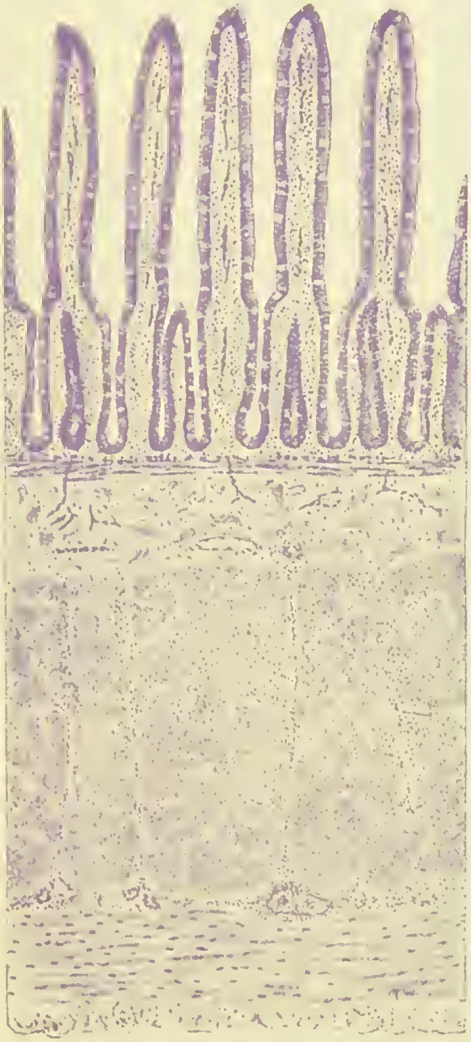

FIG. 432.—SECTION OF THE SMALL INTESTINE (JEJUNUM) OF CAT. Magnified about 40 diameters.

form the *agminated glands* or *patches of Peyer* (fig. 440). The latter occur chiefly in the ileum.

The *glands of Brunner*, which have been already noticed (p. 333), occur in the duodenum. They are small tubulo-racemose glands of serous character, situated in the submucosa (fig. 435); they send their ducts to the inner surface of the mucous membrane either between the crypts of Lieberkühn or into them.

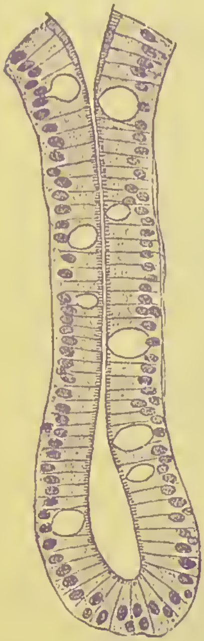

FIG. 433.

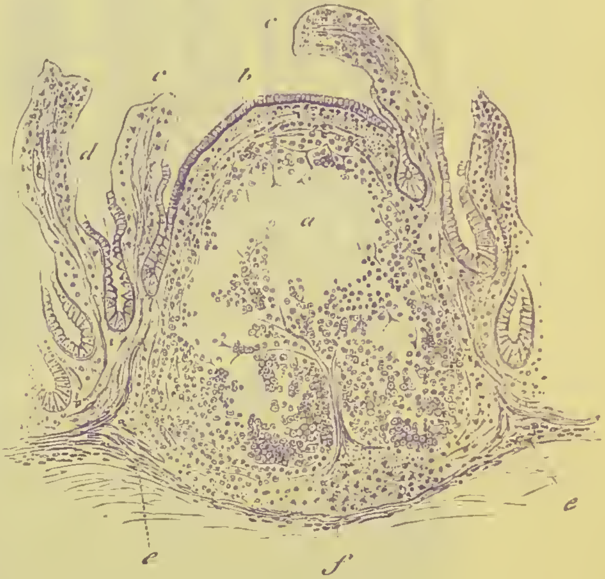

FIG. 434.

FIG. 433.—A CRYPT OF LIEBERKÜHN FROM THE HUMAN INTESTINE. (Flemming.)

FIG. 434.—SECTION OF THE ILEUM THROUGH A LYMPHOID NODULE. (Cadiat.)
a, middle of the nodule with the lymphoid tissue partly fallen away from the section; *b*, epithelium of the intestine; *c*, villi: their epithelium is partly broken away; *d*, crypts of Lieberkühn; *e*, *f*, muscularis mucosæ.

The *villi* with which the whole of the inner surface of the small intestine is closely beset are clavate or finger-shaped projections of the mucous membrane, and are composed, like that, of retiform tissue covered with columnar epithelium (figs. 436 to 438). The characters of this epithelium have already been described (Lesson VIII.). Between and at the base of the epithelium-cells many lymph-corpuscles occur, as well as in the meshes of the retiform tissue. The epithelium rests upon a basement-membrane. In the middle of the villus is a lymphatic or lacteal vessel which may be somewhat enlarged near its commencement, but the enlargement is replaced in some animals by a network of lacteals. Surrounding this vessel are small bundles of plain muscular tissue prolonged from the muscularis

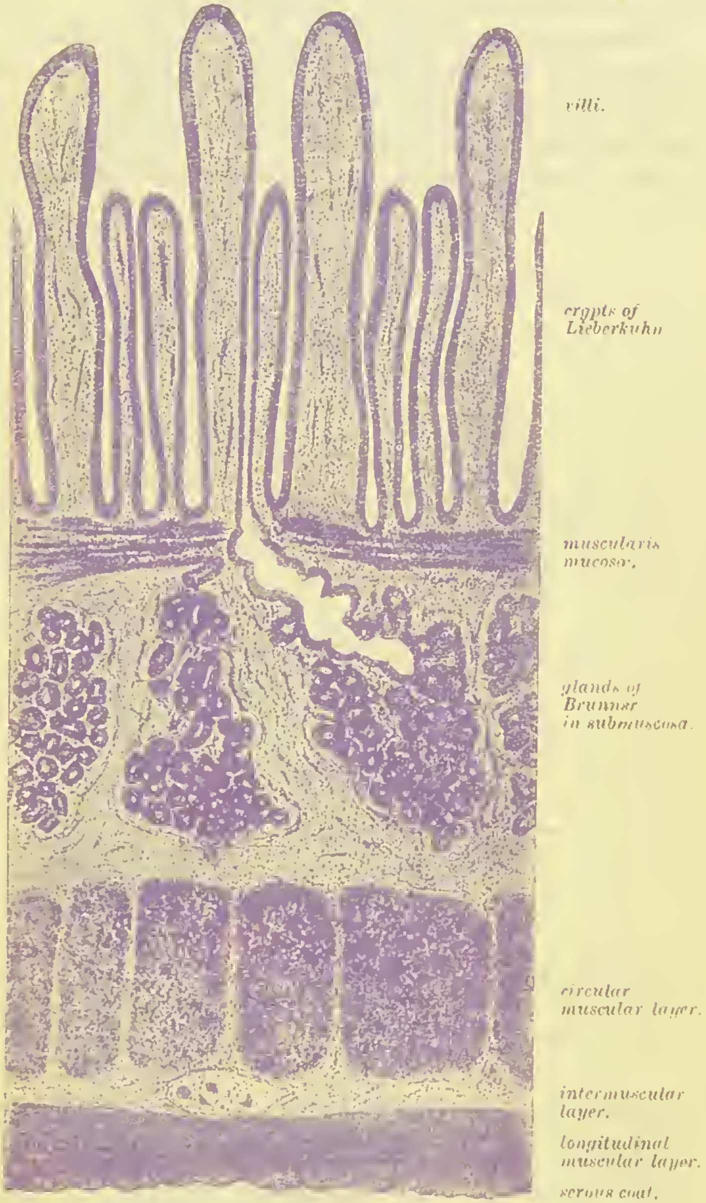

Fig. 435.—Section of duodenum of cat, showing Brunner's glands. Magnified about 60 diameters.

mucosæ. The network of blood-capillaries (figs. 436, 439) lies for the most part near the surface within the basement-membrane; it is supplied with blood by a small artery which joins the capillary network at the base of the villus; the corresponding vein generally arises near the extremity.

The *lymphatics* (lacteals) of the mucous membrane (fig. 440), after receiving the central lacteals of the villi, pour their contents into a plexus of large valved lymphatics which lie in the submucous tissue and form sinuses around the bases of the lymphoid nodules (fig. 304, p. 238). From the submucous tissue efferent vessels pass through the muscular coat, receiving the lymph from an intramuscular plexus of lymphatics, and are conveyed away between the layers of the mesentery.

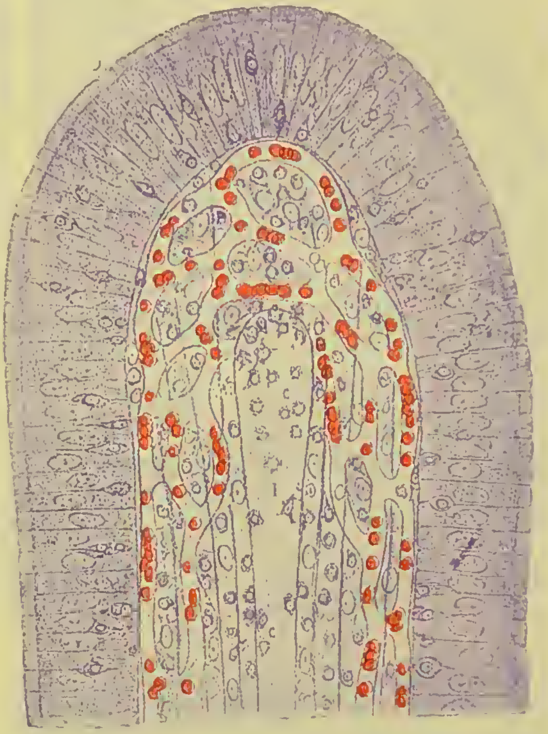

FIG. 436.—LONGITUDINAL SECTION OF A VILLUS FROM A RAT KILLED THREE HOURS AFTER FEEDING WITH BREAD AND WATER.

The columnar epithelium shows numerous lymph-corpuscles between the cells: *l*, lacteal, containing lymph-corpuscles; *c*, some partly disintegrated.

Absorption of fat.—In order to study the process of fat transference in the intestine, it is convenient to stain the fat with osmic acid, which colours it black. It can then be observed that in animals which have been fed with food containing fat, particles of fat are present (1) in comparatively large globules within the columnar epithelium cells;

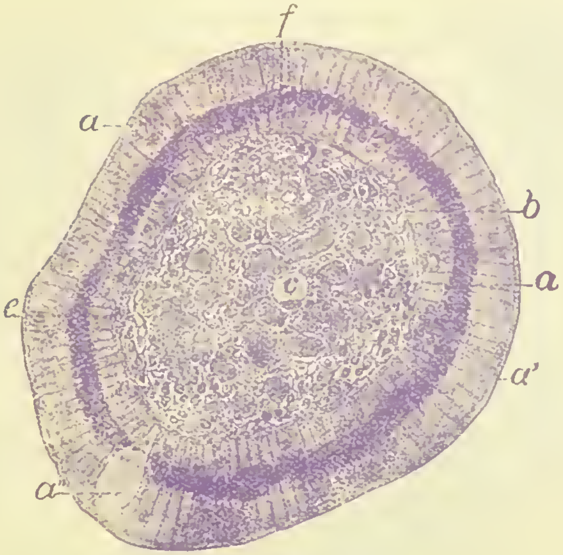

Fig. 437.—Transverse section of a villus of pig. (Trautmann.)
a, epithelium; *a′*, striated border; *a″*, goblet-cell; *b*, lymphoid tissue; *c*, small central lacteal; *e*, plain muscle-fibres cut transversely; *f*, section of arteriole.

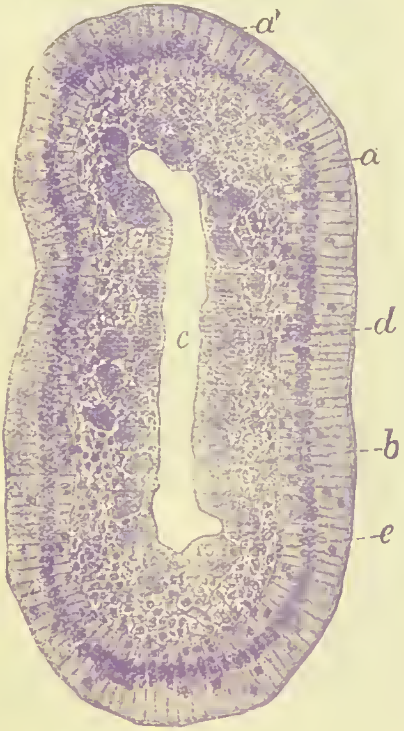

Fig. 438.—Transverse section of a villus of ox. (Trautmann.)
a, epithelium; *a′*, striated border; *b*, lymphoid tissue; *c*, large central lacteal; *e*, plain muscle-fibres cut across.

(2) in fine granules in the interstitial tissue of the villus, but often confined to the amœboid leucocytes, which abound in this tissue; (3) in fine granules within the central lacteal of the villus. The leucocytes are present not only in the reticular tissue of the villus, but also in considerable numbers between and at the base of the epithelium-cells; and they can also be seen in thin sections from bichromate-osmic preparations within the commencing lacteal; in the last situation they are undergoing disintegration (figs. 436, 441, 442). These observations are easily made in the frog.

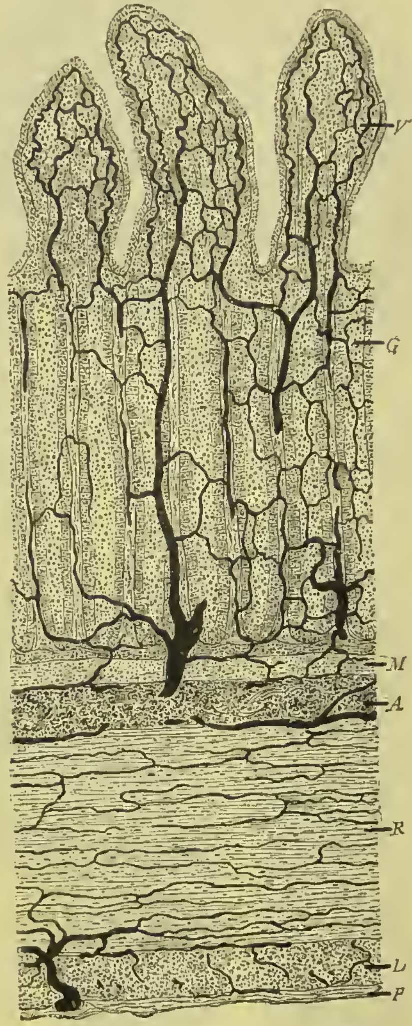

Fig. 439.—Small intestine (vertical transverse section), with the blood-vessels injected. (Heitzmann.)

V, a villus; *G*, glands of Lieberkühn; *M*, muscularis mucosæ; *A*, areolar coat; *R*, circular muscular coat; *L*, longitudinal muscular coat; *P*, peritoneal coat.

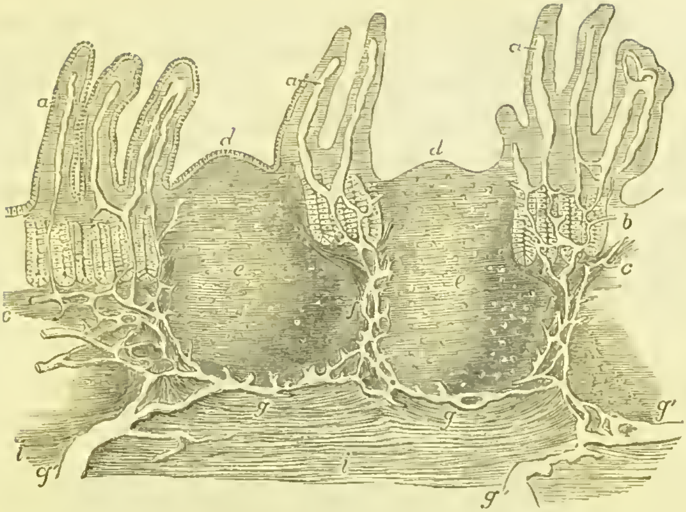

FIG. 440.—VERTICAL SECTION OF A PORTION OF A PEYER'S PATCH WITH THE LACTEAL VESSELS INJECTED. Magnified 32 diameters. (Frey.)

The specimen is from the lower part of the ileum; *a*, villi, with their lacteals left white; *b*, some of the tubular glands; *c*, the muscular layer of the mucous membrane; *d*, cupola or projecting part of the nodule; *e*, central part; *f*, the reticulated lacteal vessels occupying the lymphoid tissue between the nodules, joined above by the lacteals from the villi and mucous surface, and passing below into *g*, the sinus-like lacteals under the nodules, which again pass into the large efferent lacteals, *g'*; *i*, part of the muscular coat.

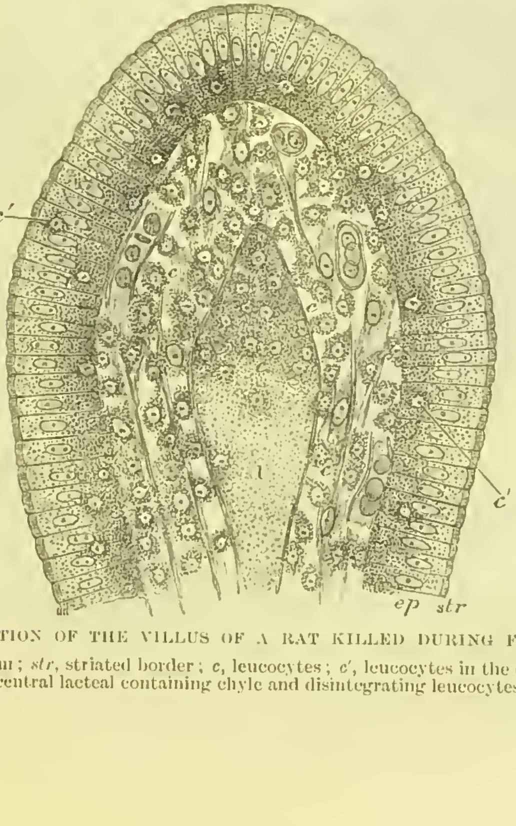

FIG. 441.—SECTION OF THE VILLUS OF A RAT KILLED DURING FAT-ABSORPTION.

ep, epithelium; *str*, striated border; *c*, leucocytes; *c'*, leucocytes in the epithelium; *l*, central lacteal containing chyle and disintegrating leucocytes.

Since the leucocytes are amœboid, it is probable from these facts that the mechanism of fat-absorption consists of the following processes —viz. (1) absorption or formation of fat in the columnar epithelium-cells of the surface; (2) ejection of fat-granules from the epithelium into the tissue of the villus; (3) inception of fat by leucocytes, these taking it up after it has passed out of the epithelium-cells; (4) migration of leucocytes carrying fat-particles through the tissue of the villus and into the central lacteal; (5) disintegration and solution of the immigrated leucocytes, and setting free their contents. Since fat-particles are never seen in the striated border of the columnar cell it is probable that the fat first becomes saponified by the action of the digestive juices, and reaches the epithelium-cell in the form of dissolved soap; the fat which is seen and stained by osmic acid within the cells having become re-formed by a process of synthesis.

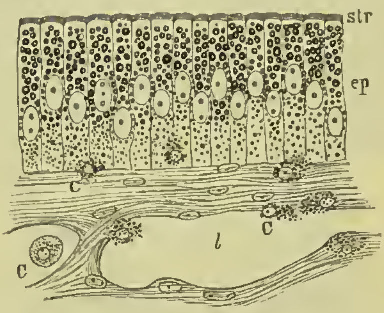

FIG. 442.—MUCOUS MEMBRANE OF FROG'S INTESTINE DURING FAT-ABSORPTION. *ep*, epithelium; *str*, striated border; *c*, leucocytes; *l*, lacteal.

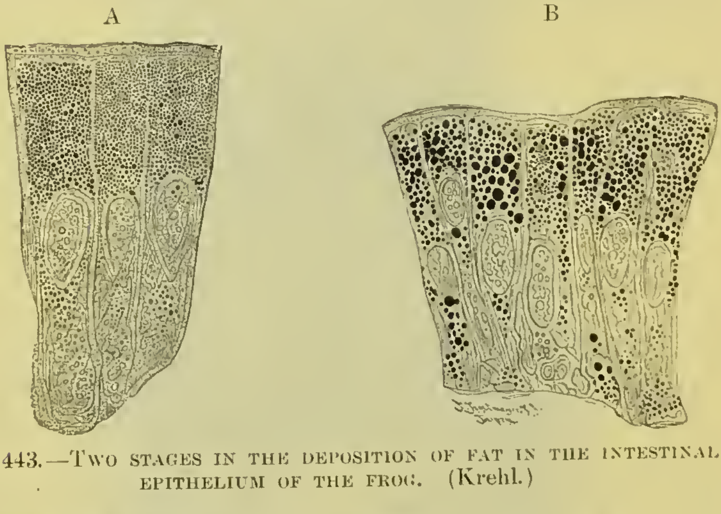

FIG. 443.—TWO STAGES IN THE DEPOSITION OF FAT IN THE INTESTINAL EPITHELIUM OF THE FROG. (Krehl.)

In some young animals (puppy, kitten) the fat which is undergoing absorption is seen not only in epithelium-cells and leucocytes, but

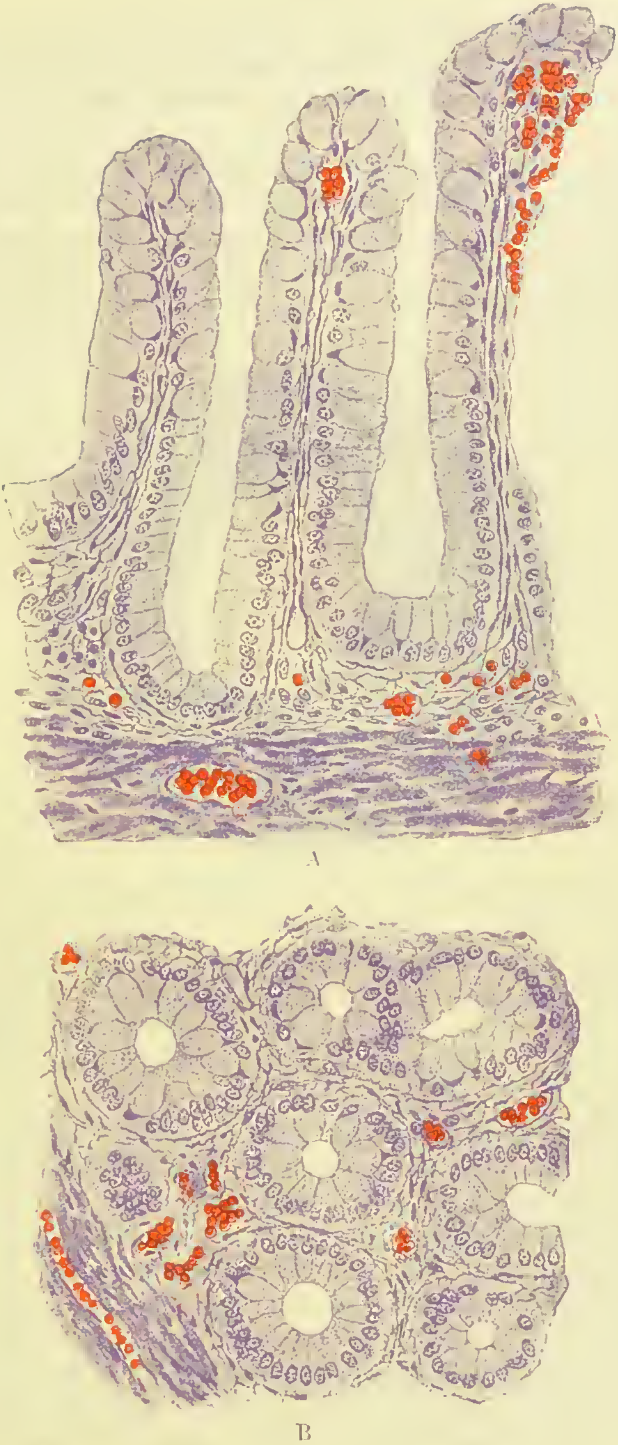

FIG. 444.—GLANDS OF THE LARGE INTESTINE OF CHILD. 300 diameters. A, in longitudinal section; B, in transverse section.

also in the form of streaks of liquid, stained black by osmic acid, in the interstices of the reticular tissue of the villi. It has probably passed out from the epithelium in a dissolved condition by a kind of reversed secretion.

The migration of leucocytes into the lacteals of the villi is not a special feature of absorption of fat, but occurs also when absorption of other matters is proceeding (fig. 436); the transference of fat-particles is merely a part of a more general phenomenon of migration of leucocytes which accompanies the process of absorption.

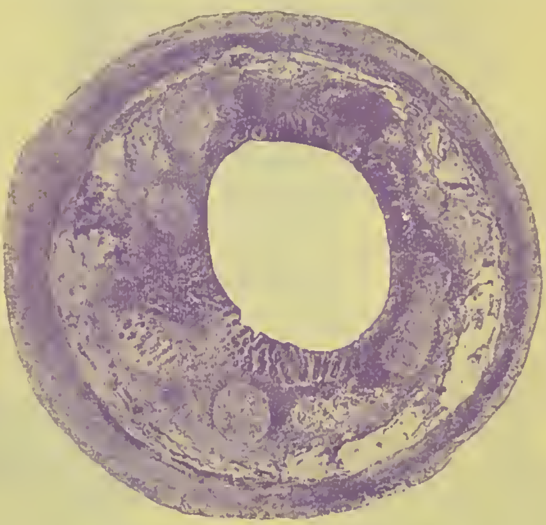

FIG. 445.—TRANSVERSE SECTION OF VERMIFORM APPENDIX. (G. Mann.)

The **large intestine** has the usual four coats, except near its termination, where the serous coat is absent. In man the *muscular coat* is peculiar in the fact that along the cæcum and colon the longitudinal muscular fibres are gathered up into three thickened bands which produce puckerings in the wall of the gut.

The *mucous membrane* of the large intestine is beset with simple tubular glands somewhat resembling the crypts of Lieberkühn of the small intestine, and lined by columnar epithelium similar to that of the inner surface of the gut, but containing many more mucus-secreting or goblet-cells (fig. 444). The blind extremity of each gland is usually slightly dilated. These glands of the large intestine are not strictly homologous with the crypts of the small intestine, for whereas the latter are developed as depressions in the general surface between the villi, the glands of the large intestine are formed by the growing together of villus-like projections of the surface. The interglandular tissue is a reticular tissue and is beset here and there with solitary glands, especially in the cæcum. The mucous membrane of the vermiform appendix (fig. 445) is in great part of its extent packed full of lymphoid nodules.

The arrangement of the blood-vessels and lymphatics in the large intestine resembles that in the stomach. The nerves of the large intestine also resemble those of the stomach and small intestine in their arrangement.

At the lower end of the rectum the circular muscular fibres of the gut become thickened a little above the anus to form the *internal sphincter* muscle. In the anal region there are a number of compound racemose mucous glands opening on the surface of the mucous membrane (*anal glands*). The anus has a lining of stratified epithelium continuous with that of the skin.

LESSONS XXXIV. AND XXXV.

THE LIVER AND PANCREAS.

1. Sections of liver are to be studied carefully. They may be stained with eosin and hæmatoxylin, or by iron-hæmatoxylin. Sketch the general arrangement of the cells in a lobule under the low power; and under the high power make very careful drawings of some of the hepatic cells and also of a portal canal. If from the pig, the outlines of the lobules are observed to be very well marked.

Notice that the hepatic cells are in intimate contact with the blood-capillaries or sinusoids. Some cells are occasionally found to contain red blood-corpuscles; many contain eosinophil granules. Notice in the sinus-like capillaries the large partly detached endothelial cells (stellate cells of Kupffer). These also frequently contain erythrocytes, which appear to be in process of destruction.

2. To observe glycogen within the liver cells, kill a rabbit or rat (preferably about six hours after a full meal of carrot), and at once throw a thin piece of the liver into 96 per cent. alcohol. When well hardened the piece may be embedded in paraffin in the usual way, or sections may be cut with the free hand without embedding. Some of the sections so obtained are to be treated with a 1 per cent. solution of iodine in potassium iodide for five minutes; they may then be mounted in a nearly saturated solution of potassium acetate, the cover-glass being cemented with gold size, but they will eventually fade.

3. Presence of iron. Other sections of alcohol-hardened liver are to be treated first with potassium ferrocyanide solution and then with hydrochloric acid and alcohol (1 to 10), passed through absolute alcohol into xylol, and mounted in dammar; in these many of the pigment granules will be stained blue (Prussian blue). Or the sections may simply be placed in an aqueous solution of hæmatoxylin (1 to 300), with or without previous treatment with alcohol containing 10 parts per cent. hydrochloric acid (to set free organically combined iron), after which they are mounted in the ordinary way (Macallum's method).

4. Injected preparations. Study with the low power a thick section to show the general arrangement of the blood-vessels, and with a high power a very thin section, which may be lightly stained with hæmatoxylin. In this the injection will be seen to have penetrated into canaliculi within the liver-cells themselves. Make a general sketch of a lobule under the low power and draw a small part of the network of blood-vessels and intracellular canaliculi under the high power.

5. Take a small piece of liver which has been several weeks in 2 per cent. bichromate of potassium solution or Müller's fluid and plunge it in 1 per cent. nitrate of silver solution, changing the fluid after half an hour. Leave the piece of liver in the silver solution overnight. It may then be transferred to alcohol, and after complete dehydration embedded and cut in paraffin in the usual way and the sections mounted in dammar. In many parts of such sections the bile-canaliculi are stained.

They can also be brought to view (at the periphery of the lobules) by injection with solution of Berlin blue from the hepatic duct; or, throughout the whole of the lobule, by injecting about 60 c.c. of saturated sulphindigotate of soda solution in three successive portions at intervals of half an hour, into the blood-vessels of an anæsthetised cat or rabbit. Two hours after the last injection the animal is killed, and the blood-vessels washed out with saturated solution of potassium chloride. The organ is then fixed with absolute alcohol. The chromate of silver method is easier and surer than the injection methods.

6. Tease a piece of fresh liver in serum or salt solution for the study of the appearance of the hepatic cells in the recent or living condition.

7. Stained sections of pancreas from a gland which has been hardened in alcohol, or in formol followed by alcohol. The sections may be stained with eosin and hæmatoxylin or with iron hæmatoxylin. Notice the islets of Langerhans between the alveoli; they are most numerous near the splenic end of the pancreas.

Make sketches under both low and high power.

8. Tease a small piece of fresh pancreas in serum or salt solution or in glycerine after osmic acid. Notice the granules in the alveolar cells, chiefly accumulated in the half of the cell which is nearest the lumen of the alveolus, leaving the outer zone of the cell clear.

Sketch a small portion of an alveolus under a high power.

9. The endings of the ducts in the alveoli, and the termination of nerve-fibres amongst the gland cells may be seen in preparations made by the Golgi method.

THE LIVER.

The **liver** is a solid glandular organ, made up of the *hepatic lobules*. These are polyhedral masses (fig. 446) about 1 mm. ($\frac{1}{25}$ inch) in diameter, composed of cells, and separated from one another by connective tissue. In some animals, as in the pig, this separation is complete, and each lobule is isolated, but in man and most animals it is incomplete. There is also a layer of connective tissue underneath the serous covering of the liver, forming the so-called *capsule* of the organ. Each lobule is penetrated by a fine network of reticular tissue which helps to support the columns of cells within the lobule (fig. 447).

The afferent **blood-vessels** of the liver (portal vein and hepatic artery) enter it on its under surface, where also the bile-duct passes away from the gland. The branches of these three vessels accompany one another in their course through the organ, and are enclosed by loose connective tissue (*capsule of Glisson*), in which are lymphatic vessels, the whole being termed a *portal canal* (fig. 448). The smaller branches of the vessels penetrate to the intervals between the hepatic lobules, and are known as the interlobular branches. The blood leaves the liver at the back of the organ by the hepatic veins; the branches of these run through the gland unaccompanied by other vessels (except lymphatics) and can also be traced to the lobules, from each of which they receive a minute branch (central or intralobular vein) which passes from the centre of the lobule, and opens directly into the (sublobular) branch of the hepatic vein.

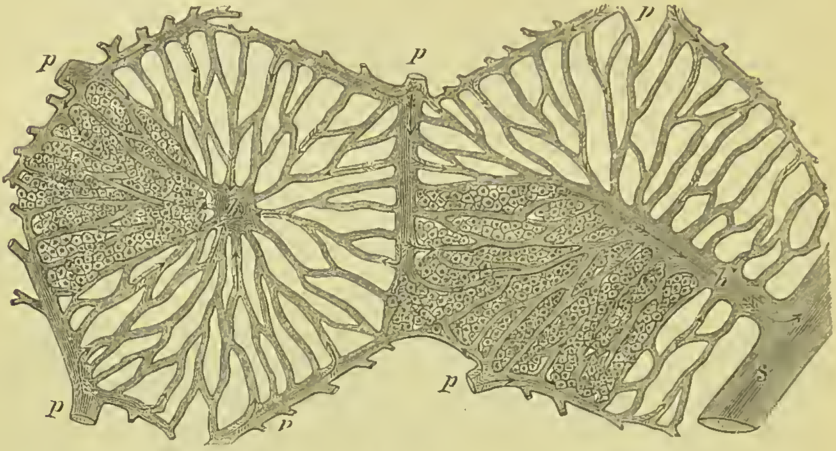

FIG. 446.—DIAGRAMMATIC REPRESENTATION OF TWO HEPATIC LOBULES.

The left-hand lobule is represented with the intralobular vein cut across; in the right-hand one the section takes the course of the intralobular vein. *p*, interlobular branches of the portal vein; *h*, intralobular branches of the hepatic veins; *s*, sublobular vein; *c*, capillaries of the lobules. The arrows indicate the direction of the course of the blood. The liver-cells are only represented in one part of each lobule.

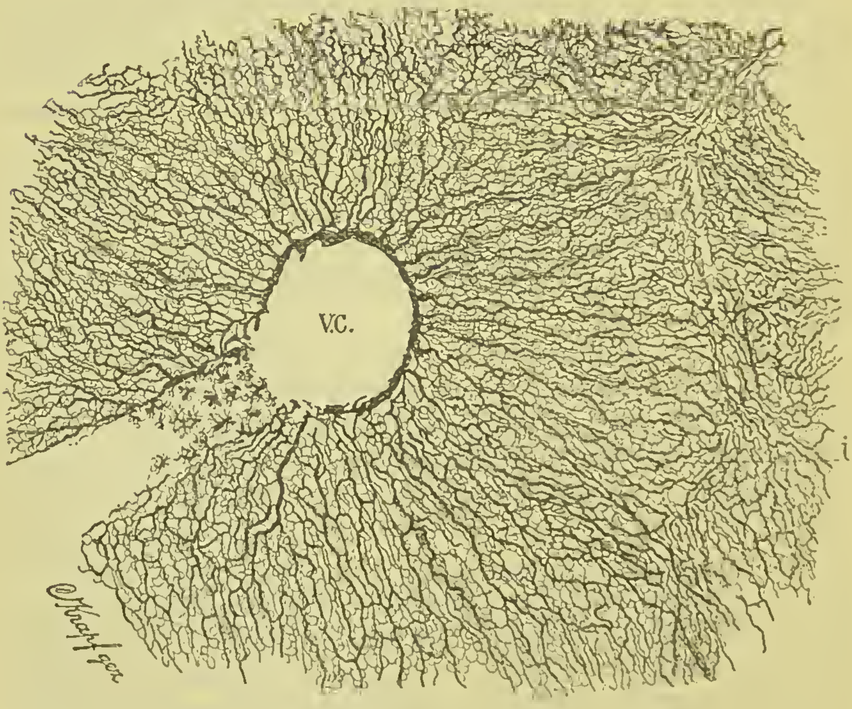

FIG. 447.—RETICULUM OF A LIVER-LOBULE. (Oppel.)

V.C., central vein; *i*, interlobular interval.

Each lobule is a mass of hepatic cells pierced everywhere with a network of sinusoid blood-vessels, the so-called hepatic capillaries (fig. 446), which at the periphery of the lobule receive blood from the interlobular branches of the portal vein (*p*), and converge to the centre of the lobule, where they unite to form the intralobular branch of the hepatic vein. The interlobular branches of the hepatic arteries join this network a short distance from the periphery of the lobule. The blood-capillaries are in direct contact with the liver cells; indeed, it would appear as if the endothelium is deficient, for artificial injections are seen to be in contact with the cells and even to pass between their interstices and run into canaliculi within their protoplasm. The endothelium of the blood-vessels (or sinusoids) is in part at least represented by certain conspicuous cells which occur at intervals on the walls of the sinusoids, and lie in contact with the liver cells. These cells were described by Kupffer. They are phagocytic, like the endothelial cells of the blood-sinuses of the spleen, and ingest erythrocytes, which can be seen within them.

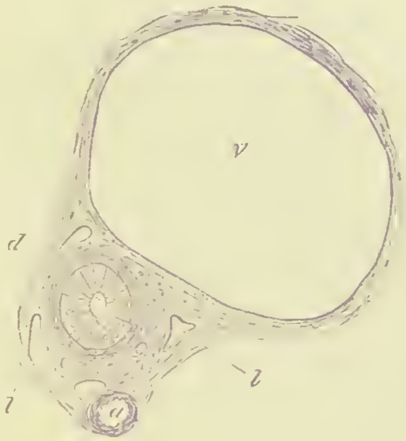

Fig. 448.—Section of a portal canal.

a, branch of hepatic artery; *v*, branch of portal vein; *d*, bile-duct; *l*, *l*, lymphatics in the areolar tissue of Glisson's capsule which incloses the vessels.

The **hepatic cells**, which everywhere lie between and surround the capillaries, are polyhedral, somewhat granularlooking cells, each containing a spherical nucleus. The protoplasm of each cell is pervaded by an irregular network of canaliculi (fig. 452), which in preparations of injected liver become filled with the injection material, which has passed into them from the blood-vessels (Herring and Simpson). They thus form a system of intracellular canals which probably receive the blood-plasma directly from the vessels. Such canals were conjectured to exist by Browicz, who showed that under certain circumstances not only hæmoglobin but whole red blood-corpuscles, and even groups of blood-corpuscles, which are in process of breaking down, are to be found in the interior of the hepatic cells. In the dog's liver both hæmoglobin and bilirubin may be found in the form of crystals within the nuclei of the liver cells (Browicz). It is easy to inject these minute canals from the blood-vessels, and they are clearly shown filled with the injection mass in the preparation of injected liver of rabbit shown in fig. 453. Besides these plasma-channels, the liver cells may show fine, short canals which communicate with the intercellular bile-ducts (see below) and generally commence within the cell by a dilatation (secretion vacuoles).

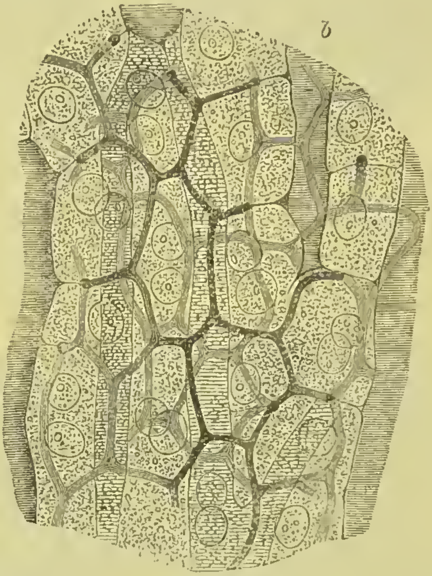

FIG. 449.—SECTION OF RABBIT'S LIVER WITH THE INTERCELLULAR NETWORK OF BILE-CANALICULI INJECTED. Highly magnified. (Herring.)

Two or three layers of cells are represented; *b*, blood-capillaries.

After a meal many of the liver cells may contain fat, and masses of glycogen can also be seen within them (fig. 454) if the liver be hardened in alcohol and treated in the manner described in section 2. The cells also contain pigment-granules, many of which are stained by potassium ferrocyanide and hydrochloric acid, or by pure hæmatoxylin (presence of iron). The iron which is in organic combination can be set free by treatment for a short time with alcohol to which 10 p.c. hydrochloric acid has been added.

The **ducts** commence between the hepatic cells in the form of *intercellular bile-canaliculi*, which lie between the adjacent sides of the cells, and receive the contents of the secretion-vacuoles above mentioned. They form a network, the meshes of which correspond in size to the cells (fig. 449), and at the periphery of the lobule they pass into the interlobular bile-ducts (fig. 450). In many animals the bile-canaliculi do not form an actual network but fine arborisations between the cells. They are always bounded by hepatic cells, never placed between a cell and a blood-capillary (G. Retzius).

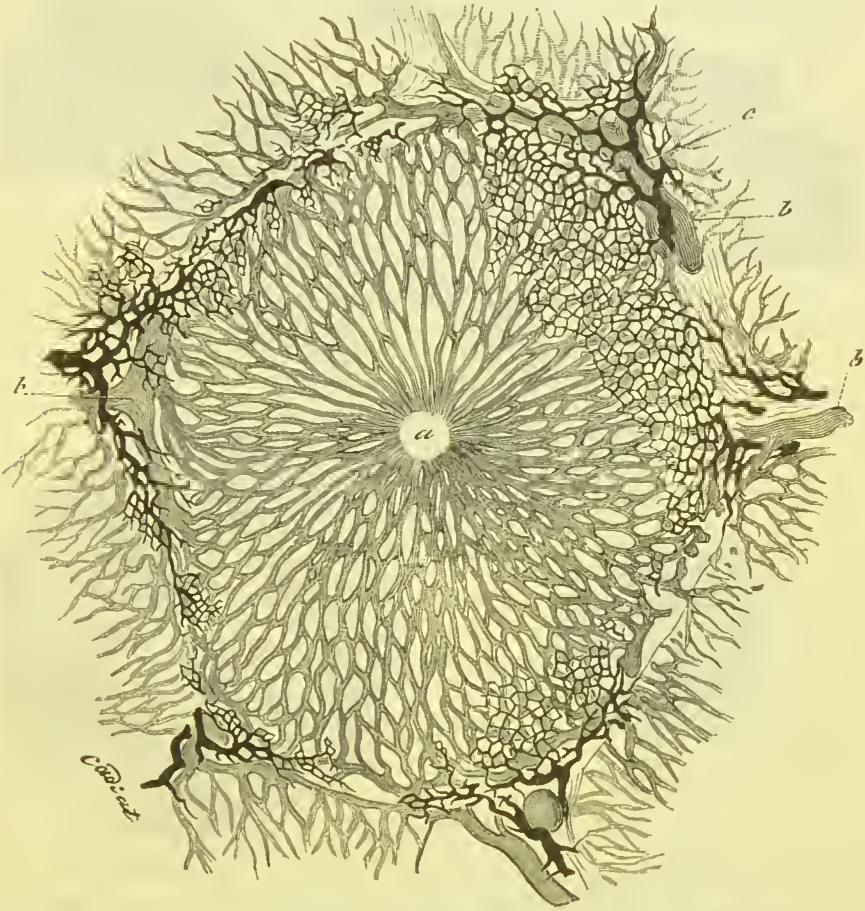

Fig. 450.—Lobule of rabbit's liver: vessels and bile-ducts injected. (Cadiat.)

a, central vein; *b*, *b*, peripheral or interlobular veins; *c*, interlobular bile-duct. The liver-cells are not represented.

The **bile-ducts** are lined by clear columnar epithelium (fig. 448, *d*). Outside this is a basement-membrane, and in the larger ducts some fibrous and plain muscular tissue. Many of the large ducts are beset with small blind diverticula.

The **gall-bladder** is in its general structure similar to the larger bile-ducts. It is lined by columnar epithelium, and its wall is formed of fibrous and muscular tissue. The mucous membrane is thrown into reticulating folds (fig. 451), which become larger and more numerous near the neck of the gall-bladder.

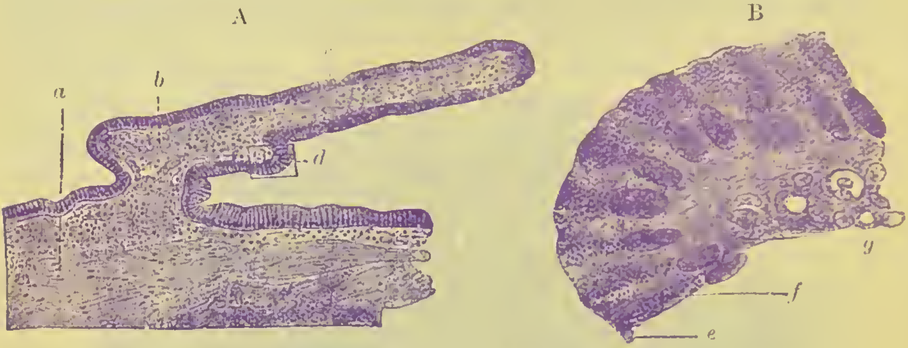

FIG. 451.—SECTIONS OF THE WALL OF THE GALL-BLADDER. (Sommer.)

A, Under a low magnifying power. *a*, muscular coat; *b*, a fold of mucous membrane; *c*, columnar epithelium; *d*, portion represented in B more highly magnified.
B, Magnified portion of epithelium and subjacent corium. *e*, striated border; *f*, mucigen granules in cells; *g*, blood-capillaries.

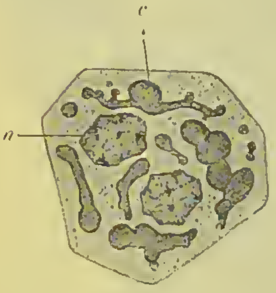

FIG. 452.

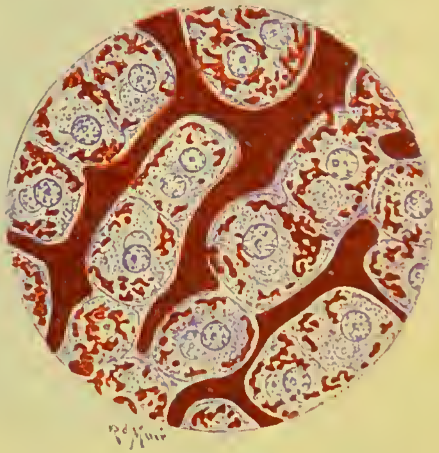

FIG. 453.

FIG. 452.—A CELL FROM THE HUMAN LIVER, SHOWING INTRACELLULAR CANALICULI. (Browicz.)

FIG. 453.—FROM A SECTION OF RABBIT'S LIVER INJECTED FROM THE PORTAL VEIN, SHOWING INTRACELLULAR CANALICULI COMMUNICATING WITH THE INTERCELLULAR BLOOD-SINUSOIDS.

The **lymphatics** of the liver have been described as commencing as perivascular lymphatic spaces inclosing the capillaries of the lobules (MacGillavry). But this cannot be so, since there is no space between the liver cells and the sinusoid capillaries with which they come into immediate relationship (Herring and Simpson). All that can be positively asserted is that there are numerous lymphatics accompanying the branches of the portal vein, and others, less numerous, accompanying the tributaries of the hepatic veins, but so far as can be ascertained no direct communication exists between the two sets of lymphatics within the lobules, although they communicate freely both at the periphery of the lobules and near their exit from the liver. Most of the lymph passes out by the portal lymphatics.

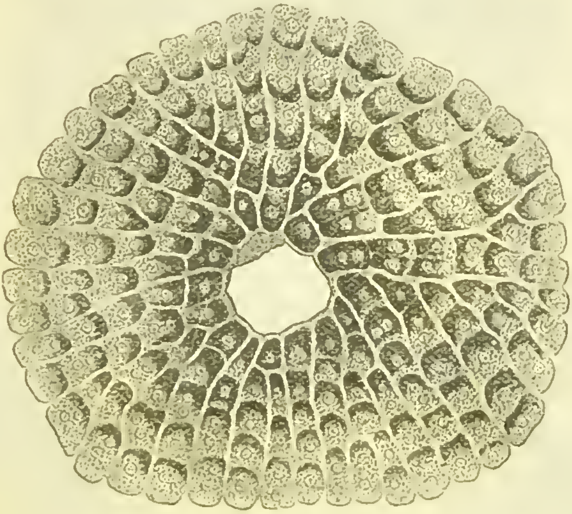

FIG. 454.—LIVER CELLS CONTAINING GLYCOGEN. (Barfurth.)

Nerves are described as distributed both to the blood-vessels and to the liver cells.

THE PANCREAS.

The **pancreas** is a tubulo-racemose gland, resembling the salivary glands so far as its general structure is concerned, but differing from them in the fact that the alveoli are longer and more tubular in character. Moreover, the connective tissue of the gland is somewhat looser, and there occur in the glandular substance here and there small groups of epithelium-like cells unfurnished with ducts (*islets of Langerhans*) (fig. 455, *a*; fig. 456), which are supplied with a close network of large convoluted capillary vessels (fig. 457). Their function is unknown, but their presence is very characteristic of the pancreas. The degeneration which they sometimes undergo in cases of diabetes mellitus (as well as other considerations) seems to suggest that they are concerned with the influence exerted by the pancreas on the metabolism of carbohydrates.

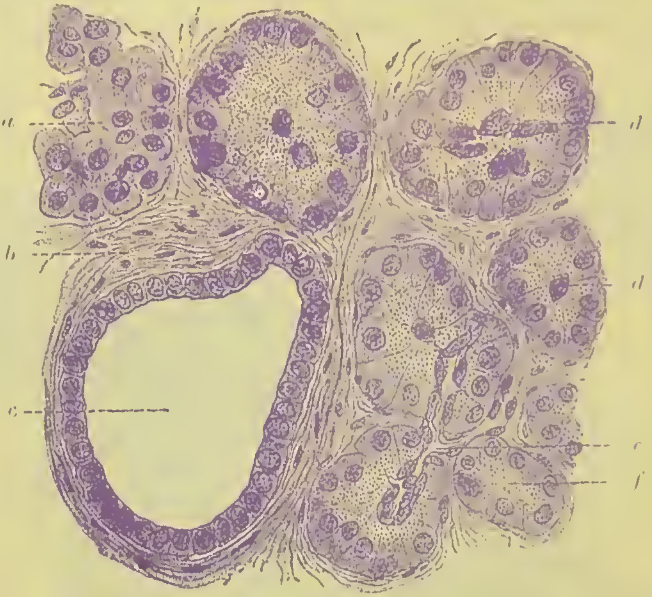

FIG. 455.—SECTION OF HUMAN PANCREAS. (Böhm and v. Davidoff.) $\frac{450}{1}$.

a, group of cells in interstitial tissue (islet of Langerhans); *b*, connective tissue; *c*, larger duct; *d*, *d*, alveoli with centro-acinar cells; *e*, small duct passing into alveoli; *f*, inner granular zone of alveolus.

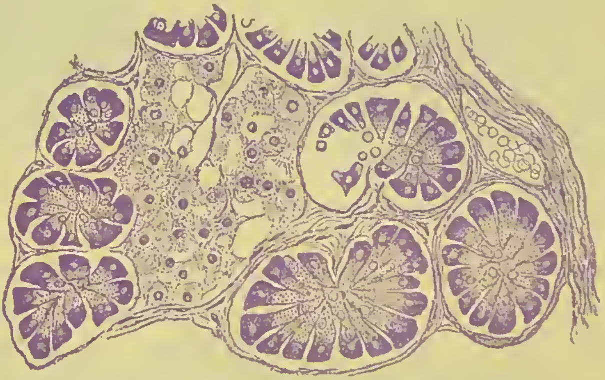

FIG. 456.—SECTION OF PANCREAS OF ARMADILLO SHOWING SEVERAL ALVEOLI AND A LARGE INTERALVEOLAR CELL-ISLET. (V. D. Harris.)

The cells of the alveoli are shrunken, but they show markedly the two zones, the outer or non-granular stained deeply by hæmatoxylin.

The cells which line the alveoli are columnar or polyhedral in shape. When examined in the fresh condition, or in sections stained by certain reagents (*e.g.* osmic acid), their protoplasm is seen to be

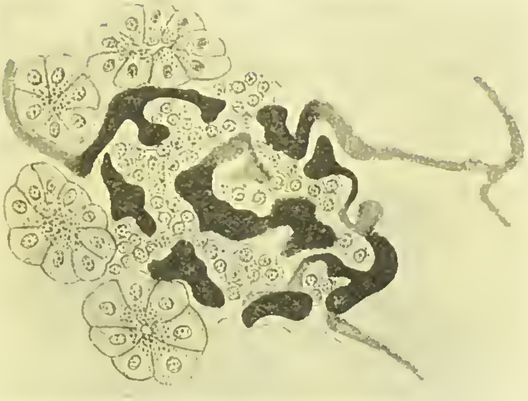

FIG. 457.—INJECTION OF BLOOD-VESSELS OF AN "ISLET" OF THE PANCREAS. (Kühne and Lea.)

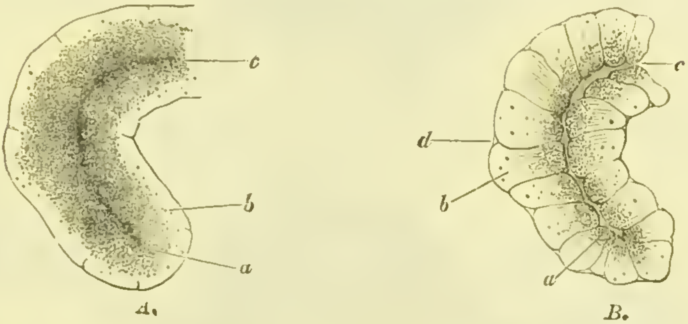

FIG. 458.—PART OF AN ALVEOLUS OF THE RABBIT'S PANCREAS. *A*, AT REST; *B*, AFTER ACTIVE SECRETION. (From Foster, after Kühne and Lea.)

a, the inner granular zone, which in *A* is larger and more closely studded with granules than in *B*, in which the granules are fewer; *b*, the outer transparent zone, small in *A*, larger in *B*, and in the latter marked with faint striæ; *c*, the lumen, very obvious in *B*, but indistinct in *A*; *d*, indentation at the junction of two cells, only distinct in *B*.

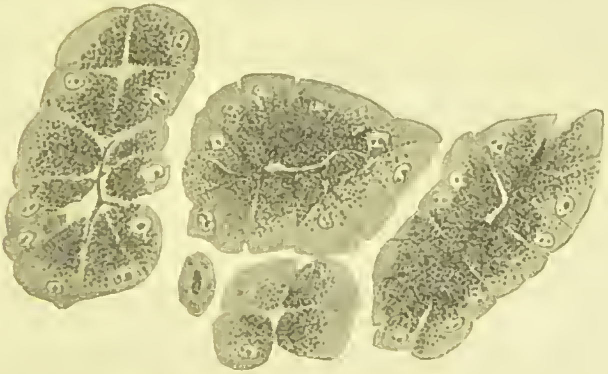

FIG. 459.—ALVEOLI OF DOG'S PANCREAS, CELLS LOADED.

filled in the inner two-thirds with granules, but the outer third is left clear or is striated (fig. 455, 458, *A*; figs. 459). After a period of activity the clear part of the cell becomes larger, and the granular part smaller (figs. 458, *B*; fig. 460). In hæmatoxylin-stained sections the outer part is coloured more deeply than the inner (fig. 456).

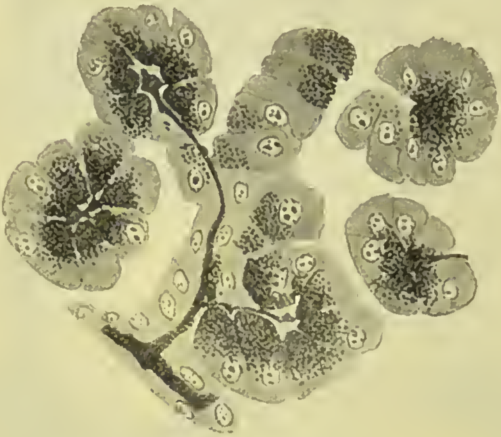

FIG. 460.—ALVEOLI OF DOG'S PANCREAS AFTER A PERIOD OF ACTIVITY PRODUCED BY APPLICATION OF ACID TO MUCOUS MEMBRANE OF DUODENUM.

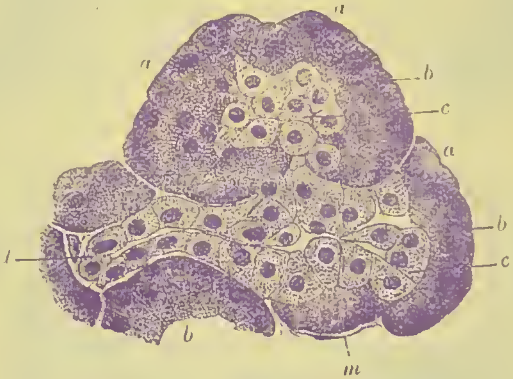

FIG. 461.—FROM A SECTION OF HUMAN PANCREAS. (v. Ebner.) Magnified 530 diameters.

a, *a*, outer zones of alveolar cells with striated appearance; *b*, inner granular zones; *m*, membrana propria; *c*, centro-acinar cells, here occurring in unusually large amount; *d*, junctional part of duct; its epithelium is continuous with the centro-acinar cells.

Pancreas cells frequently exhibit a rounded mass of granules or fibrils (mitochondria) near the nucleus, which is known as the paranucleus: this is probably related to the secretory activity of the cells.

In the centre of each acinus there may generally be seen some spindle-shaped cells (*centro-acinar cells* of Langerhans—fig. 455, *d*), the nature of which has not been definitely determined; but they appear to be continued from the cells which line the smallest ducts (fig 455, *e*). Sometimes they are much more conspicuous, and fill the parts of the alveoli which are nearest to the duct (fig. 461); in these cases the mass of cells which they form is liable to be mistaken for a Langerhans' islet.

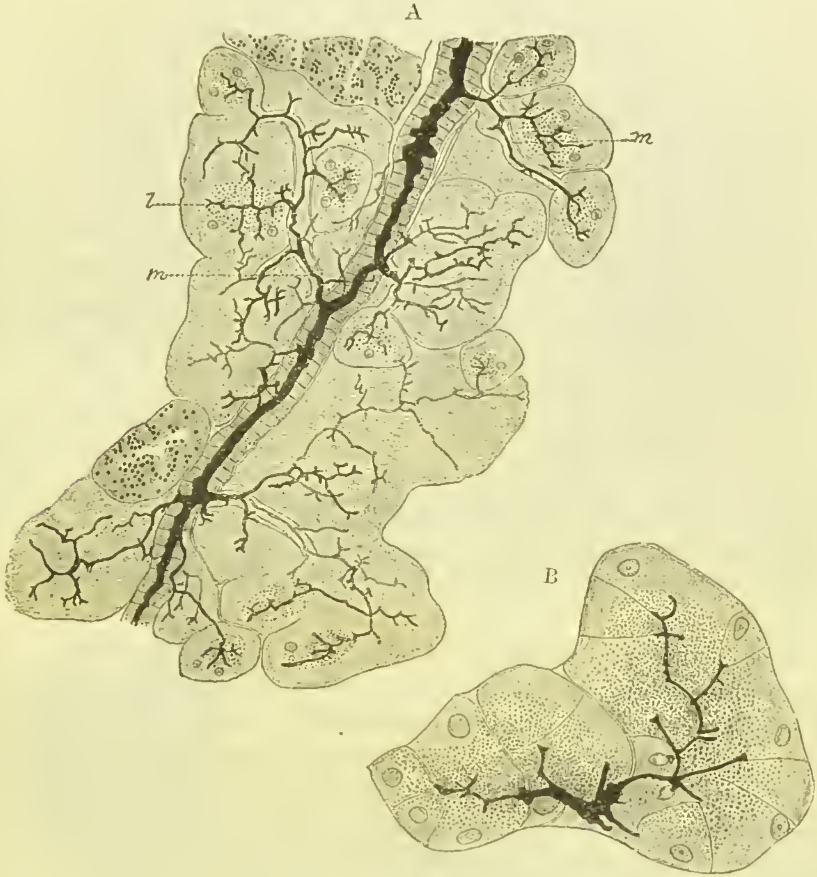

FIG. 462.—A DUCT OF THE PANCREAS WITH LATERAL DIVERTICULA INTO THE ALVEOLI; GOLGI METHOD. (E. Müller.)

In *A* the duct is shown cut longitudinally and giving off ductules, *m*, to the alveoli, where they extend between the cells (*l*). In *B* the details of their termination are shown more highly magnified.

Diverticula from the lumen of the alveolus penetrate between the alveolar cells (fig. 462). The pancreas has many nerves, with numerous small nerve cells distributed upon their course; the nerve-fibrils end by ramifying amongst the cells of the alveoli, as in the salivary glands. In the cat, which has Pacinian bodies in its mesentery, these terminal organs are also found numerously in the substance of the pancreas (V. D. Harris).

LESSON XXXVI.

STRUCTURE OF THE KIDNEY.

1. Sections passing through the whole kidney of a small mammal, such as a mouse or rat. The sections will show the general arrangement of the organ and the disposition of the tubules and of the Malpighian corpuscles.

2. Thin sections of the kidney of a larger mammal, such as the dog or cat, may next be studied. In some the direction of the section should be parallel with the rays of the medulla, and in others across their direction. The characters of the epithelium of the several parts of the uriniferous tubules and the structure of the glomeruli are to be made out in these sections.

3. Separate portions of the uriniferous tubules may be studied in teased preparations from a kidney which has been macerated in strong hydrochloric acid for a few hours. This renders it possible to unravel the uriniferous tubules for some distance.

4. Thick sections of a kidney in which the blood-vessels have been injected. Examine these with a low power of the microscope. Follow the course of the arteries—those to the cortex sending their branches to the glomeruli, those to the medulla rapidly dividing into pencils of fine vessels which run between the straight uriniferous tubules of the boundary zone. Notice also the efferent vessels from the glomeruli breaking up into the capillaries which are distributed to the tubules of the cortical substance.

The **kidney** is a compound tubular gland. To the naked eye it appears formed of two portions—a *cortical* and a *medullary* (fig. 463). The latter is subdivided in man into about twelve pyramidal portions (*pyramids of Malpighi*), the base (boundary zone) of each being surrounded by cortical substance, while the apex projects in the form of a *papilla* into the dilated commencement of the ureter (*pelvis of the kidney*).[1] Both cortex and medulla are composed entirely of tubules—the *uriniferous tubules*—which have a straight direction in the medulla and a contorted arrangement in the cortex; but groups of straight tubules also pass from the medulla through the thickness of the cortex (*medullary rays*) (figs. 463, 464).

The **uriniferous tubules** begin in the cortical part of the organ in dilatations, each inclosing a tuft or glomerulus of convoluted capillary blood-vessels (*corpuscles of Malpighi*), the dilated commencement of the tubule being known as the *capsule* (fig. 467, M). The *glomerulus* is lobulated (figs. 465, 466); the lobules being united by the afferent and efferent vessels and covered by a flattened epithelium reflected

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[1] In many animals (*e.g.* dog, cat, rabbit, and monkey) the whole kidney is formed of only a single pyramid, but in other animals the pyramids are even more numerous than in man.

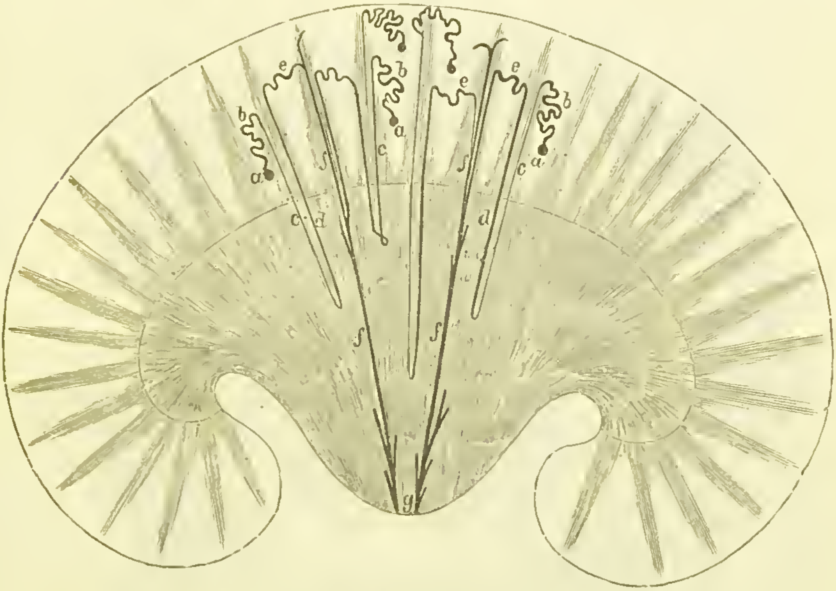

Fig. 463.—Diagram of the course of the tubules in a unipyramidal kidney, such as that of the rabbit. (Toldt.)

a, Malpighian bodies; *b*, first convoluted tubule; *c*, *d*, looped tube of Henle; *e*, second convoluted; *f*, collecting tube; *g*, ducts of Bellini.

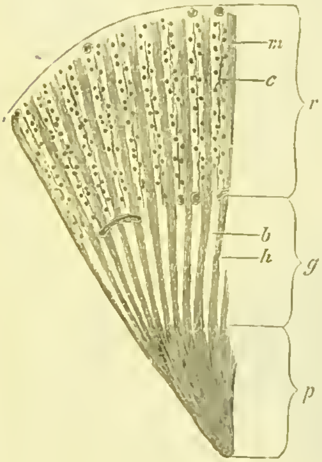

Fig. 464.—Section through part of a dog's kidney. (Ludwig.)

p, papillary, and *g*, boundary zones of the medulla; *r*, cortical layer; *h*, bundles of tubules in the boundary layer, separated by spaces, *b*, containing bunches of vessels (not here represented), and prolonged into the cortex as the medullary rays, *m*; *c*, intervals of cortex, composed chiefly of convoluted tubules, with irregular rows of glomeruli, between the medullary rays.

from that lining the capsule. The glomeruli near the medulla are larger than the rest and have more lobules. The capillary-wall in all the glomeruli is a syncytium, showing no cell-outlines in silver preparations (Drasch).

The *tubule* leaves the capsule by a *neck* (fig. 467, *n*) which is rarely narrower than the rest of the tubule in mammals. In some animals (*e.g.*

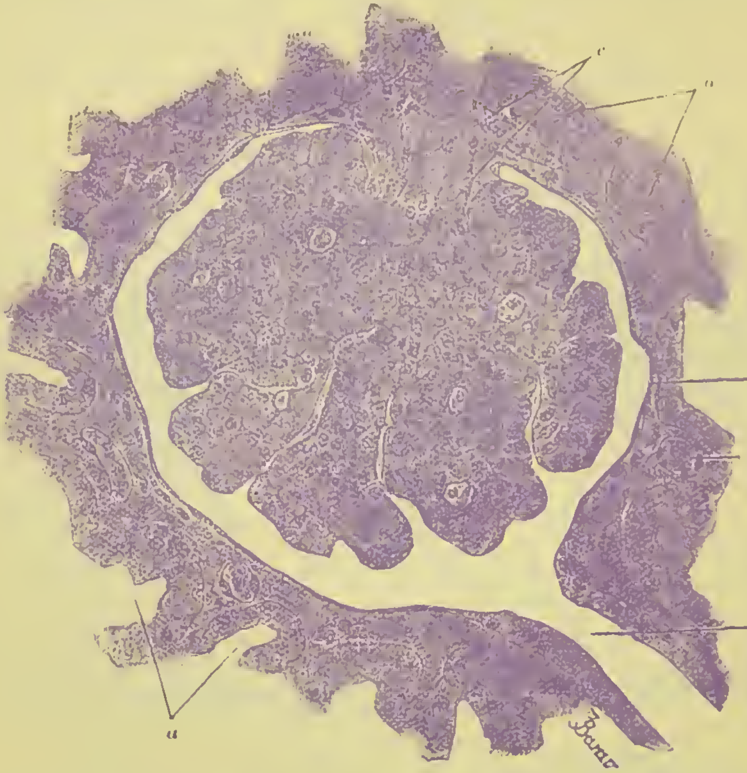

Fig. 465.—A malpighian corpuscle from the kidney of the monkey. (Szymonowicz.) Magnified 350 diameters.

a, *a*, sections of convoluted tubules; *a′*, commencement of convoluted tube from capsule; *b*, capsule; *c*, afferent and efferent vessels of glomerulus.

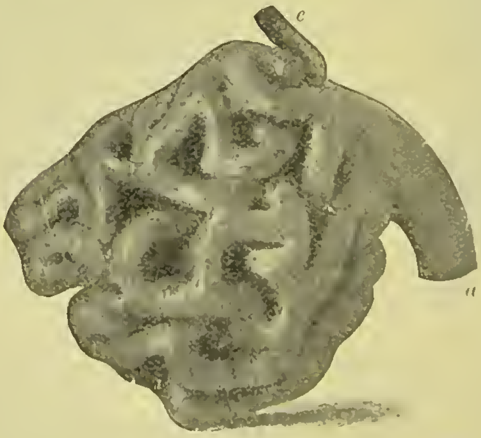

Fig. 466.—Model of a glomerulus. (Johnston.)

a, afferent; *c*, efferent blood-vessel.

frog) the neck is long, and has ciliated epithelium. The tubule is at first convoluted (*first or distal convoluted tubule*). It then becomes nearly straight or slightly spiral only (*spiral tubule*), and rapidly narrowing passes down into the medulla towards the dilated commencement of the

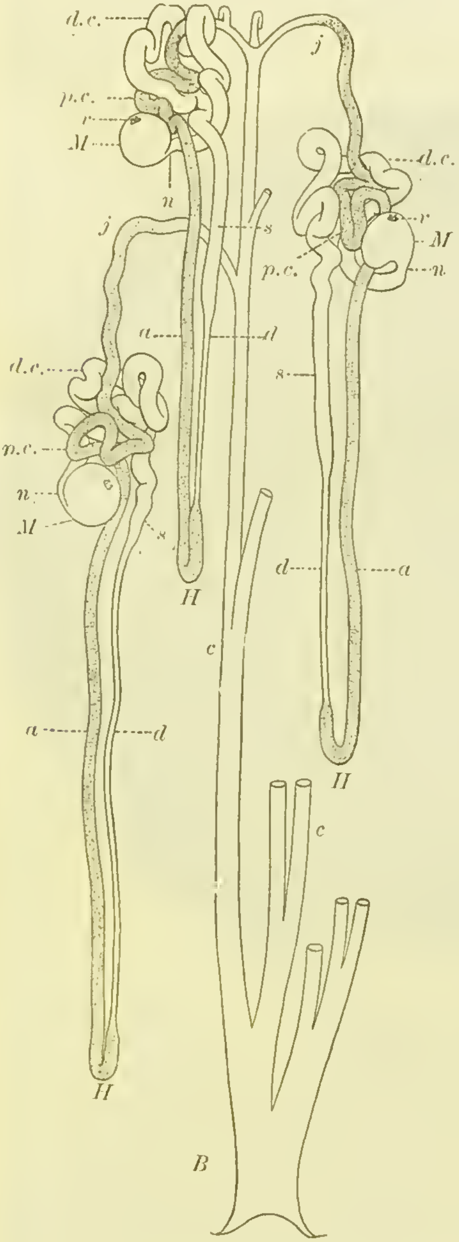

FIG. 467.—PLAN OF THE ARRANGEMENT OF THE URINIFEROUS TUBULES. (Huber.)

M, Malpighian corpuscles; *v*, point of entrance of vessels of glomerulus; *n*, neck; *d.c.*, distal convoluted tubule, which arises from the Malpighian corpuscle; *s*, spiral tubule into which it is continued; *d*, narrow descending limb of loop of Henle; *H*, loop of Henle (this is sometimes formed by the narrow part of the looped tubule, but is here represented as formed by the wider part); *a*, wider ascending limb of loop of Henle; this passes back to the neighbourhood of the same Malpighian corpuscle, often becoming irregular and zigzag at its upper end. Here it becomes continuous with the proximal convoluted tubule, *p.c.*, which eventually passes into the junctional tubule, *j*, by which it is connected with a collecting tubule, *c*. *B*, duct of Bellini, receiving a number of conjoined collecting tubules and opening at a papilla.

ureter as the *descending limb of the looped tubule of Henle.* It does not at once, however, open directly into the pelvis of the kidney, but before reaching the end of the papilla it turns round in the form of a loop (*loop of Henle*), and passes upwards again towards the cortex, parallel to its former course, and larger than before (*ascending limb of looped tubule of Henle*). Arrived at the cortex it approaches close to the capsule from which the tubule took origin. but at a point opposite to the origin, viz. near the afferent and efferent vessels of the glomerulus (Golgi). It then becomes larger and irregularly zigzag (*zigzag or irregular tubule*), and again somewhat convoluted (*second or proximal convoluted tubule*). Eventually it straightens out again and narrowing

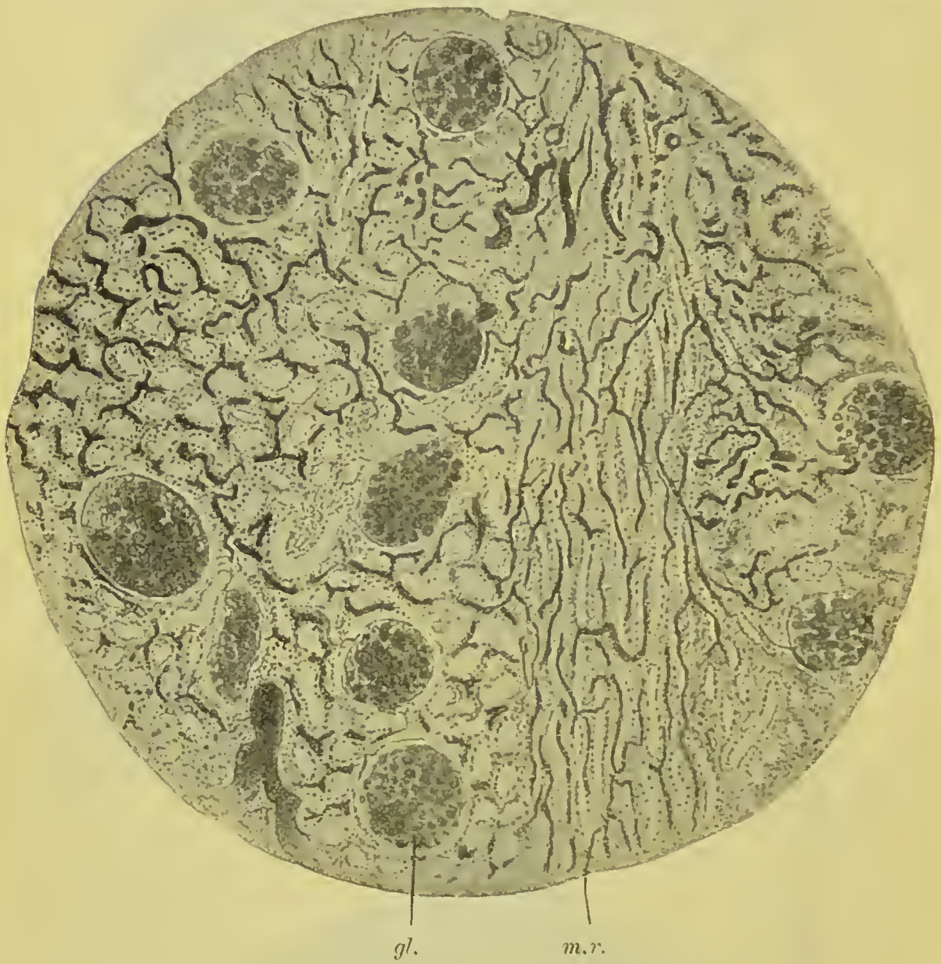

FIG. 468.—PART OF A SECTION THROUGH THE CORTEX OF A HUMAN KIDNEY, THE BLOOD-VESSELS OF WHICH HAVE BEEN INJECTED. (Disse.)

gl., a glomerulus; *m.r.*, section of a medullary ray.

into a small vessel (*junctional tubule*), joins a *straight or collecting tubule*. The last-named unites with others to form larger collecting tubes which pass through the medullary substance of the kidney to open at the apex of the papilla as the *ducts of Bellini* (fig. 472).[1]

The tubules are throughout bounded by a basement-membrane, which is lined by epithelium, but the characters of the epithelium-cells vary in the different parts of a tubule. In the *capsule* (fig. 465), the epithelium is flattened and is reflected over the glomerulus. In some animals (*e.g.* mouse) the granular epithelium of the convoluted tube is prolonged a little way into the capsule. In the first *convoluted* and *spiral tubules* the epithelium is thick, and the cells are markedly granular, with a tendency for the granules to be arranged in lines perpendicular to the basement-membrane (rodded or fibrillar appear-

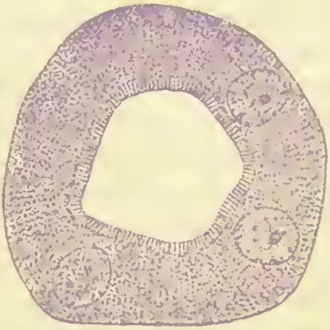

FIG. 469.—SECTION OF A CONVOLUTED TUBULE OF THE RABBIT'S KIDNEY, SHOWING THE STRUCTURE OF THE EPITHELIUM. (Szymonowicz). Magnified 1100 diameters.

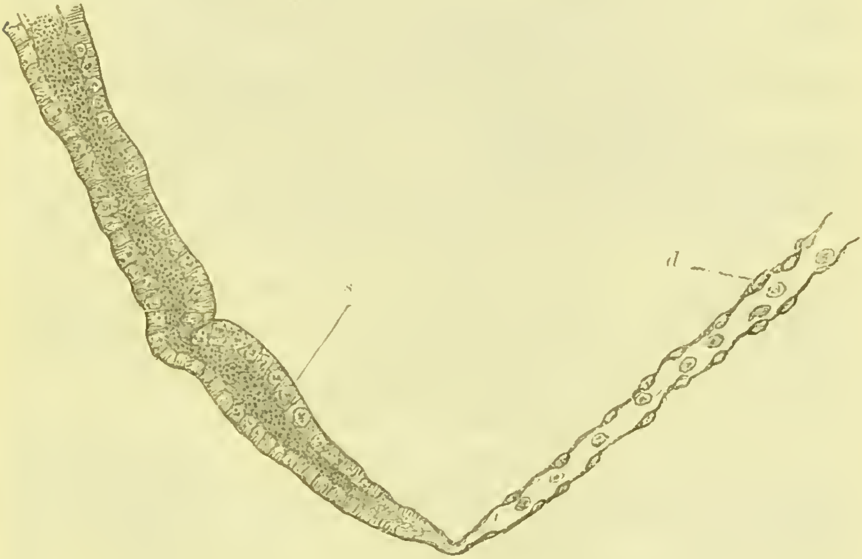

FIG. 470.—PASSAGE OF THE SPIRAL CONTINUATION OF A DISTAL CONVOLUTED TUBULE INTO THE DESCENDING LIMB OF A LOOPED TUBULE OF HENLE. (Disse.) The bend is accidental.

s, end of spiral tubule ; *d*, narrow descending limb of looped tubule of Henle.

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[1] The terms *distal* and *proximal* as applied to the convoluted tubules are sometimes used in a sense the reverse of that here employed.

ance, fig. 469). The granules of the cells are eosinophil. The cells often exhibit a brush of cilium-like processes projecting into the lumen (fig. 469), but these are not vibratile. In the narrow *descending limb of the looped tubules*, and in the loop itself, the cells are clear and flattened (fig. 469), and leave a relatively large lumen ; in the *ascending limb* they again acquire a granular or fibrillar structure and may nearly fill the lumen. The arrangement of the cell-granules in lines perpendicular to the basement-membrane is still more marked in the *zigzag tubules*, and a similar structure is present also in the *second convoluted tubules*, into which these pass. On the other hand, the *junctional tubule* has a larger lumen and in it the granular striated epithelium gives place to clear flattened cells. The *collecting tubes* have also a very distinct lumen and are lined by clear cubical or columnar epithelium cells (fig. 471, *a*).

The following gives a tabular view of the parts which compose a uriniferous tubule, and the nature of the epithelium in each part:

PORTION OF TUBULE.	NATURE OF EPITHELIUM.	POSITION OF TUBULE.
Capsule . . .	Flattened, reflected over glomerulus, where its cells are said to form a syncytium.	Labyrinth of cortex.[1]
Distal convoluted tubule	Cubical, granular, with appearance of fibrillation ("rodded"), the cells interlocking.	Labyrinth of cortex.
Spiral tubule . .	Like the last	Medullary ray of cortex.
Descending limb of looped tubule.	Clear flattened cells	Boundary zone and partly papillary zone of medulla.
Loop of Henle . .	Like the last (or may be like the ascending limb).	Papillary zone of medulla.
Ascending limb of looped tubule.	Cubical, granular; the cells sometimes imbricated.	Medulla, and medullary ray of cortex.
Zigzag tubule . .	Cells strongly "rodded": varying height, lumen small.	Labyrinth of cortex.
Proximal convoluted tubule.	Similar to distal convoluted tube, but cells are longer, with larger nuclei, and they have a more refractive aspect.	Labyrinth of cortex.
Junctional tubule .	Clear flattened and cubical cells .	Labyrinth, passing to medullary ray.
Straight or collecting tubule.	Clear cubical and columnar cells .	Medullary ray and medulla.
Duct of Bellini . .	Clear columnar cells	Opens at apex of papilla.

Blood-vessels.—The renal artery divides into branches on entering the organ, and these branches pass towards the cortex, forming incomplete arches between the cortex and the medulla (fig. 473, *a*). The branches of the renal vein form similar but more complete arches (*g*). From the arterial arches vessels pass through the cortex

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[1] The part of the cortex between and surrounding the medullary rays is so named.

(*cortical or interlobular arteries, b*), and give off at intervals (in some animals from one side only) small arterioles (*afferent vessels of the glomeruli*), each of which enters the dilated commencement of a uriniferous tubule, within which its capillaries form a glomerulus. From the glomerulus a somewhat smaller *efferent vessel* passes out, and this at once again breaks up into capillaries, which are distributed amongst the tubules of the cortex (*e*); their blood is collected by veins which run parallel with the cortical arteries but not in juxtaposition with them: these veins join the venous arches between the cortex and the medulla; they receive blood from certain other veins which arise by radicles having a somewhat stellate arrangement near the capsule (*venæ stellulæ, j*).

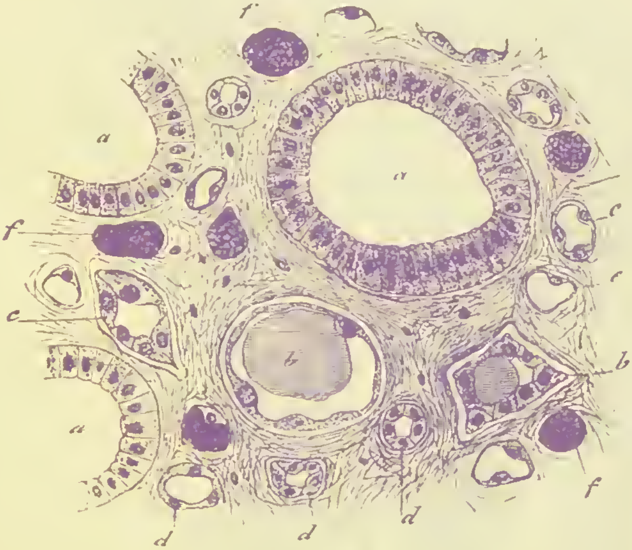

FIG. 471.—SECTION ACROSS A PAPILLA OF THE KIDNEY. (Cadiat.)
a, large collecting tubes (ducts of Bellini); *b*, *c*, *d*, tubules of Henle; *e*, *f*, blood-capillaries.

The medulla derives its blood-supply from special offsets of the arterial arches, which almost immediately break up into pencils of fine straight arterioles running in groups between the straight tubules of the medulla. These arterioles supply a capillary network with elongated meshes which pervades the medulla (fig. 473, *f*), and which terminates in a plexus of somewhat larger venous capillaries in the papillæ. From these and from the other capillaries the venules of the medulla collect the blood, and pass, accompanying the straight arterioles, into the venous arches between the cortex and medulla. The groups of small arteries and veins (*vasa recta*) in the part of the medulla nearest to the cortex alternate with groups of the uriniferous tubules, and this arrangement confers a striated aspect upon this portion of the medulla (*boundary zone*, fig. 464, *g*).

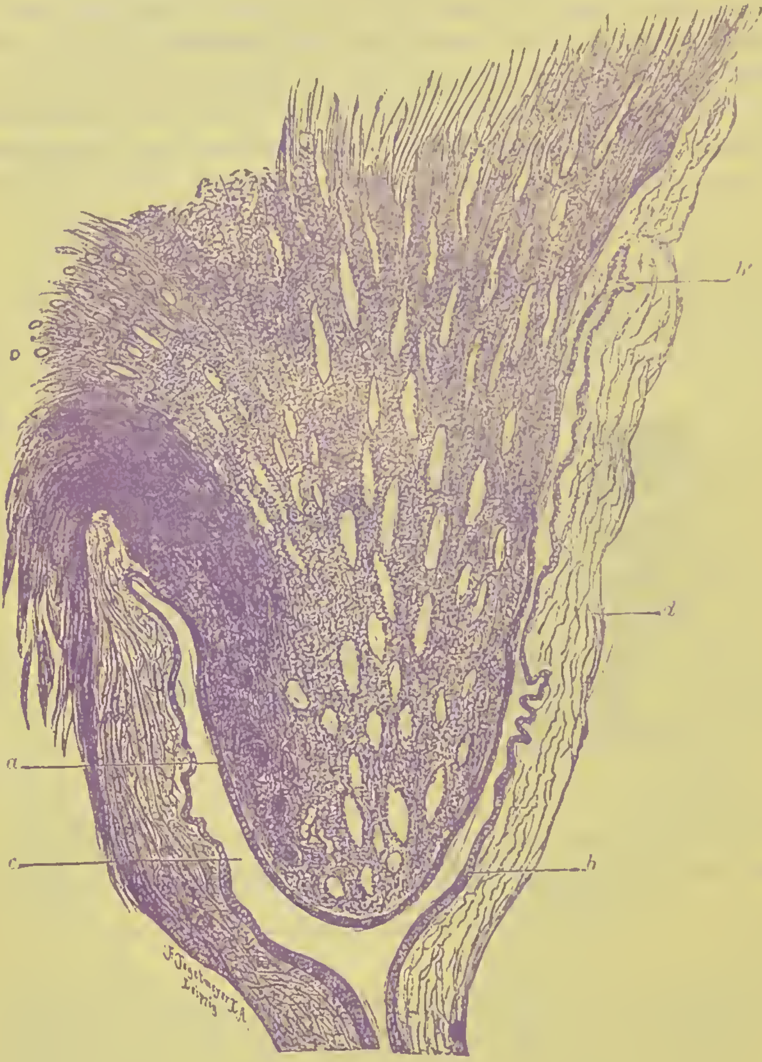

FIG. 472.—LONGITUDINAL SECTION THROUGH A PAPILLA OF THE KIDNEY SHOWING ITS PROJECTION AT ONE OF THE CALICES OF THE KIDNEY-PELVIS. (Disse.)

The ducts of Bellini are seen cut obliquely; the smaller tubules are looped tubules of Henle. *a*, epithelium covering papilla; *b*, epithelium lining calix; *c*, cavity of calix; *d*, connective tissue.

The efferent vessels of those glomeruli which are situated nearest to the medulla also break up into pencils of fine vessels (*false vasa recta*) which join the capillary network of the medulla (fig. 473, *d*).

Between the uriniferous tubules, and supporting the blood-vessels, is a certain amount of connective tissue (fig. 471), which contains cleft-like lymphatics.

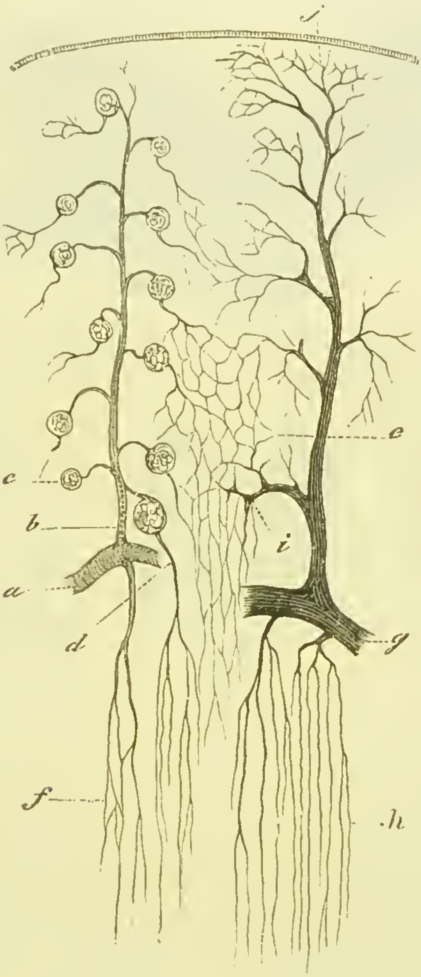

FIG. 473.—VASCULAR SUPPLY OF KIDNEY. (Cadiat.)

a, part of arterial arch; *b*, interlobular artery; *c*, glomerulus; *d*, efferent vessel passing to medulla as false arteria recta; *e*, capillaries of cortex; *f*, capillaries of medulla; *g*, venous arch; *h*, straight veins of medulla; *j*, vena stellula; *i*, interlobular vein.

Nerve-fibrils are described as ramifying amongst the epithelium-cells of the tubules (fig. 474), but most of the nerves to the kidneys are distributed to the blood-vessels.

Development of the uriniferous tubules.—The ducts of Bellini and the collecting tubules are derived as hollow sprouts from the enlarged upper end of the ureter, which in its turn is formed as a bud from the Wolffian duct of the embryo. The rest of the uriniferous tubules, including the Malpighian corpuscle, is formed from a hollow S-shaped island of cells

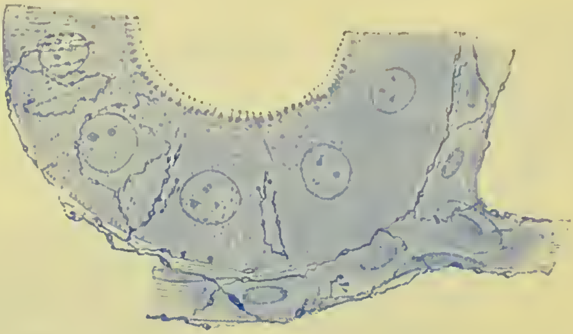

FIG. 474.—NERVE FIBRILS ENDING OVER CAPILLARY BLOOD-VESSELS AND AMONGST THE EPITHELIUM CELLS OF A CONVOLUTED TUBE OF THE FROG'S KIDNEY. (Smirnow.)

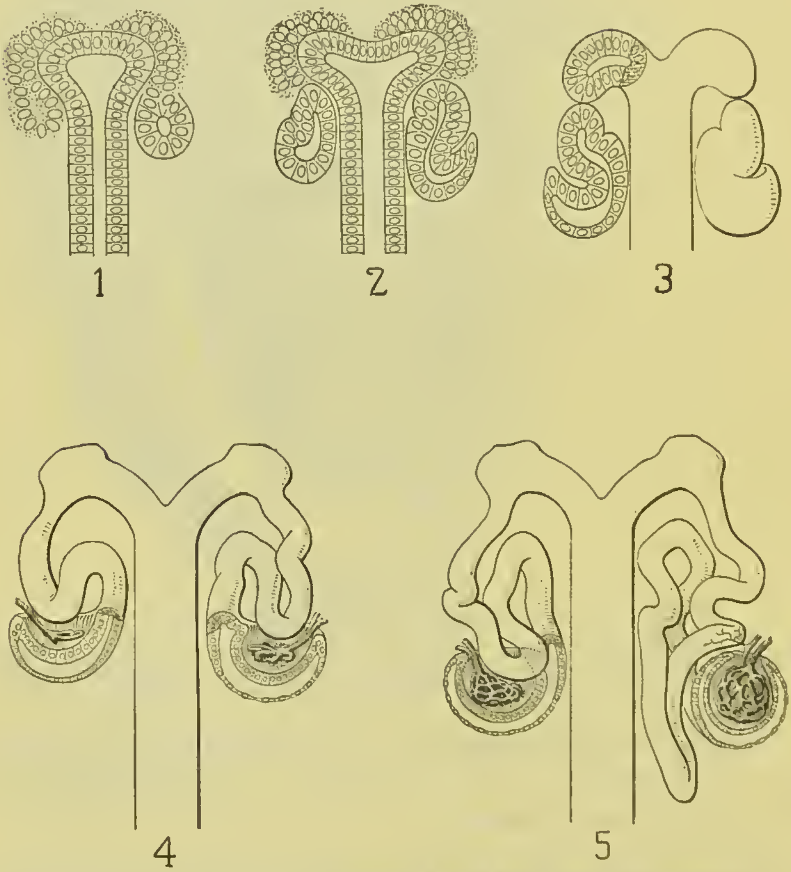

FIG. 475.—FIVE DIAGRAMS TO ILLUSTRATE THE MODE OF DEVELOPMENT OF THE URINIFEROUS TUBULES AND THE GLOMERULI. (Huber.)

which become differentiated in the mesoderm near the blind end of a collecting tubule. The lower part of the S forms a spoon-shaped structure, within the bowl of which the vessels of the glomeruli become developed; the sides of the bowl then grow round and completely inclose them. The upper part of the S forms a convoluted tubule which before long makes connection with the previously blind end of the forked collecting tubule. At first there is no sign of the looped tubule, but this presently grows down from the convoluted tubule, very much as if a part of this tube had been drawn out towards the papilla. The several stages of formation of the uriniferous tubule are shown in the diagrams marked 1 to 5 in fig. 475. These diagrams exhibit nine stages of development of the tubules, since in every one, except diagram 3, an earlier stage is represented upon the left-hand side, and a later upon the right-hand side.

LESSON XXXVII.

STRUCTURE OF THE URETER, BLADDER, AND MALE GENERATIVE ORGANS.

1. Section across the lower part of the ureter. Another section may be taken across the upper part near the pelvis of the kidney.

2. Section of the urinary bladder vertical to the surface.

In the sections of the ureter and of the urinary bladder, notice the transitional epithelium resting on a mucous membrane, which is composed of areolar tissue without glands (in most animals), and the muscular coat outside this. In the ureter there is a layer of connective tissue outside the muscular coat, and at the upper part of the bladder a layer of serous membrane covering the muscular tissue.

3. Section across the penis (child or monkey). The blood-vessels of the organ should be injected with the hardening fluid so as the better to exhibit the arrangement of the venous spaces which constitute the erectile tissue. Notice the large venous sinuses of the corpora cavernosa and the smaller spaces of the corpus spongiosum, in the middle of which is seen the (flattened) tube of the urethra.

4. Section across urethra and prostate gland (child or monkey). Notice the glandular tubes and the plain muscular tissue of the prostate, and the character of the urethral epithelium.

5. Section of testis and epididymis. The sections may be made from a rat's testis which has been hardened in alcohol; they can be stained with iron-hæmatoxylin. In these sections notice the strong capsule surrounding the gland, the substance of which consists of tubules which are variously cut; and the epithelium of the tubules, which is in different phases of development in different tubules. Observe the strands of polyhedral interstitial cells, much more numerous in some animals, lying in the loose tissue between the tubules; also the lymphatic clefts in that tissue. Notice in sections through the epididymis the epithelium of that tube.

Sketch carefully under a high power the contents of some of the seminiferous tubules to illustrate the mode of formation of the spermatozoa.

6. Examination of spermatozoa. Spermatozoa may be obtained fresh from the testicle or seminal vesicles of a recently killed mammal and examined in saline solution. Their movements may be studied on the warm stage; to display their structure a very high power of the microscope is necessary. They may be preserved and stained as "film" preparations, as with marrow (p. 32).

The **ureter** (fig. 476) is a muscular tube lined by mucous membrane. The *muscular coat* consists of two layers of plain muscular tissue, an outer circular, and an inner longitudinal. In the lower part there are some longitudinal bundles external to the circular. Outside the muscular coat is a layer of connective tissue in which the blood-vessels and nerves ramify before entering the muscular layer.

The *mucous membrane* is composed of areolar tissue, and is lined by transitional epithelium, like that of the bladder.

The **urinary bladder** has a muscular wall lined by a strong mucous membrane and covered in part by a serous coat.

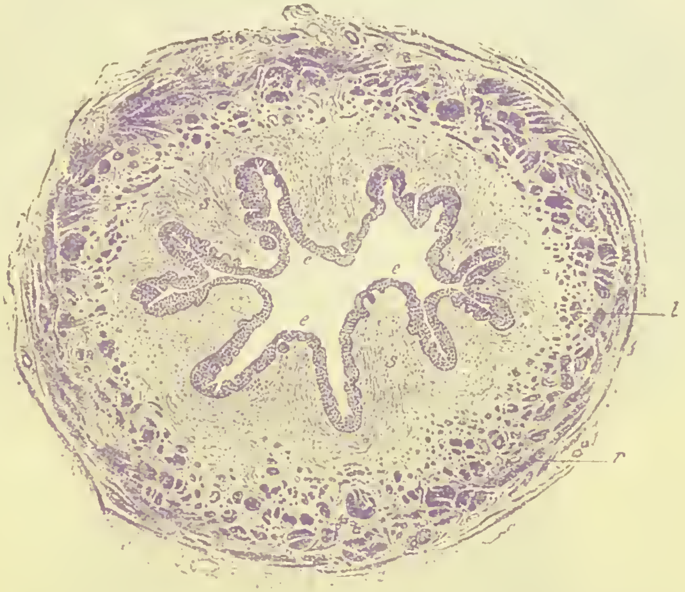

Fig. 476. Section across the upper part of the ureter. (v. Ebner.) Magnified 14 diameters.

e, epithelium; *s*, mucous membrane; *l*, longitudinal muscle; *r*, circular muscle.

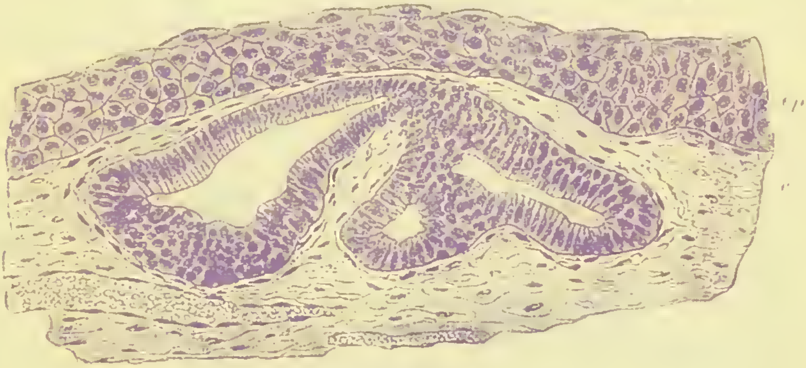

Fig. 477.—Section of part of wall of base of bladder, human. (Lendorf.) Magnified 230 diameters.

The section passes through a glandular invagination of the epithelium. *ep*, epithelium; *c*, corium.

The *muscular coat* consists of three layers, but the innermost is incomplete. The principal fibres run longitudinally and circularly, and the circular fibres are collected into a layer of some thickness which immediately surrounds the commencement of the urethra. The *mucous membrane* is lined by a transitional stratified epithelium (figs. 477, 478). The shape and structure of the cells have already been studied (p. 67). Many of the superficial cells have two nuclei. Near the base of the bladder gland-like invaginations of the epithelium are occasionally found (fig. 477), and in the bladder of some animals well-marked glands are constantly found.

The *nerves* to the bladder form gangliated plexuses, and are distributed to the muscular tissue and blood-vessels: some are said to enter the epithelium.

The **penis** is mainly composed of cavernous tissue which is collected into two principal tracts—the *corpora cavernosa*, one on each side, and the *corpus spongiosum* in the middle line inferiorly. All these are bounded by a strong capsule of fibrous and plain muscular tissue, containing also many elastic fibres and sending in strong septa or trabeculæ of the same tissues, which form the boundaries of the cavernous spaces of the erectile tissue (fig. 480). The arteries of the tissue run in these trabeculæ, and their capillaries open into the cavernous spaces. On the other hand, the spaces are connected with efferent veins. The arteries of the cavernous tissue may sometimes in injected specimens be observed to form looped or twisted projections into the cavernous spaces (*helicine arteries of Müller*), into which they may open directly.

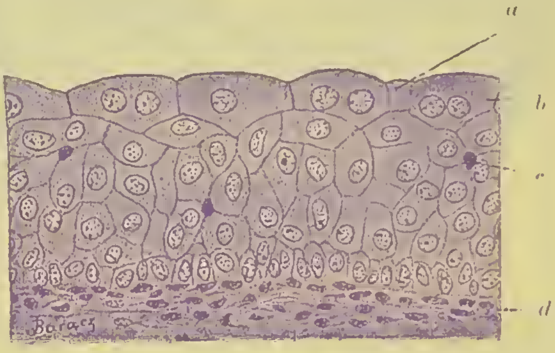

FIG. 478.—SECTION OF THE MUCOUS MEMBRANE OF THE BLADDER TO SHOW ITS EPITHELIUM. (Szymonowicz.)

a, *b*, superficial epithelium-cells; *c*, leucocyte; *d*, connective tissue of mucous membrane.

The integument of the penis and clitoris, especially that of the glans, contains numerous special nerve end-organs of the nature of end-bulbs (see p. 191), and Pacinian bodies are also found upon the nerves. Lymphatic vessels are numerous in the integument of the organ and also in the submucous tissue of the urethra.

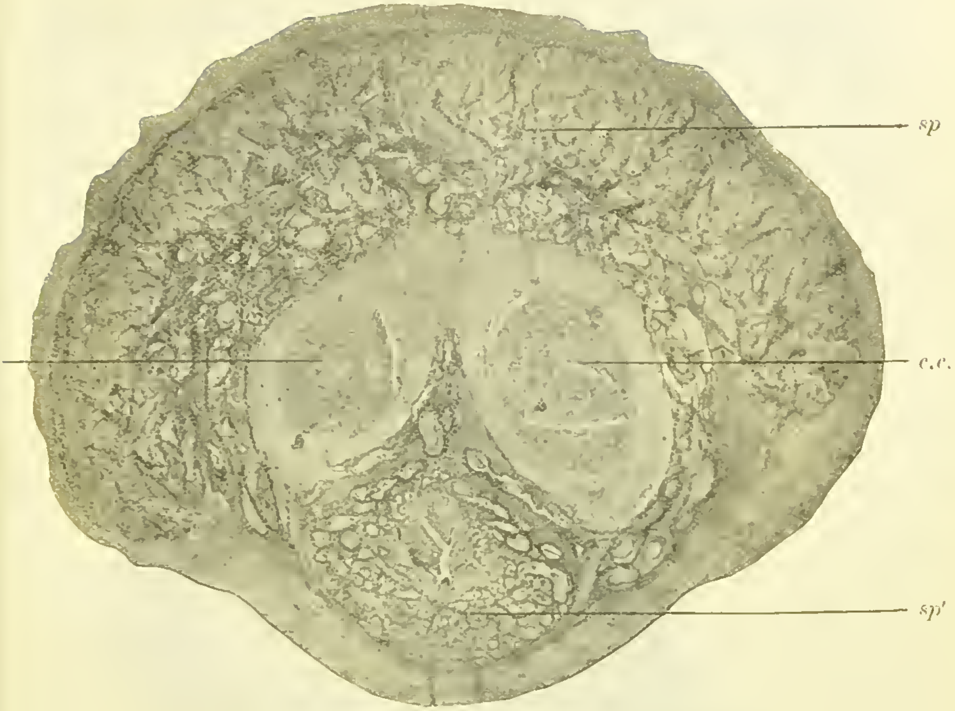

FIG. 479.—TRANSVERSE SECTION OF GLANS PENIS OF CHILD. (Rothfeld.)

c.c., corpora cavernosa ; *sp*, corpus spongiosum ; *sp′*, corpus spongiosum urethræ, with the lumen of the urethra in the centre appearing as an irregular slit with folded walls.

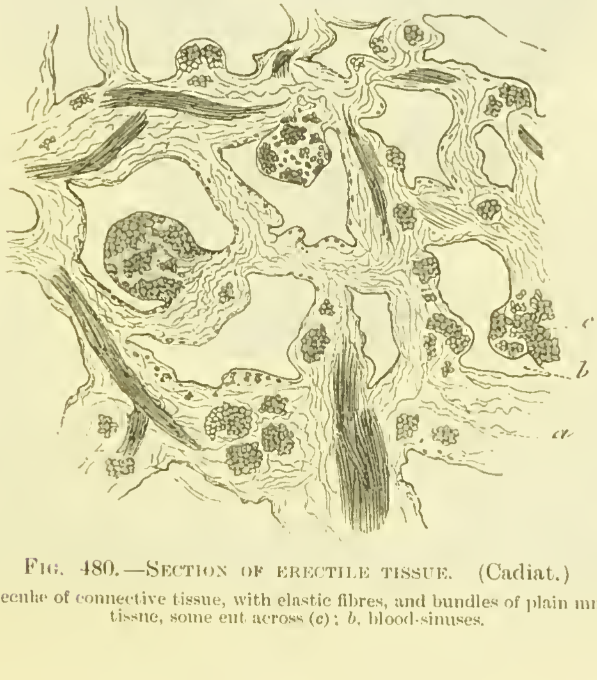

FIG. 480.—SECTION OF ERECTILE TISSUE. (Cadiat.)

a, trabeculæ of connective tissue, with elastic fibres, and bundles of plain muscular tissue, some cut across (*c*) ; *b*, blood-sinuses.

Urethra.—The cross-section of the urethra appears in the middle of the corpus spongiosum in the form of a cleft (fig. 479). It is lined in the prostatic part by transitional, but elsewhere by columnar epithelium, except near its orifice, where the epithelium is stratified. In the female urethra the epithelium is stratified throughout. The

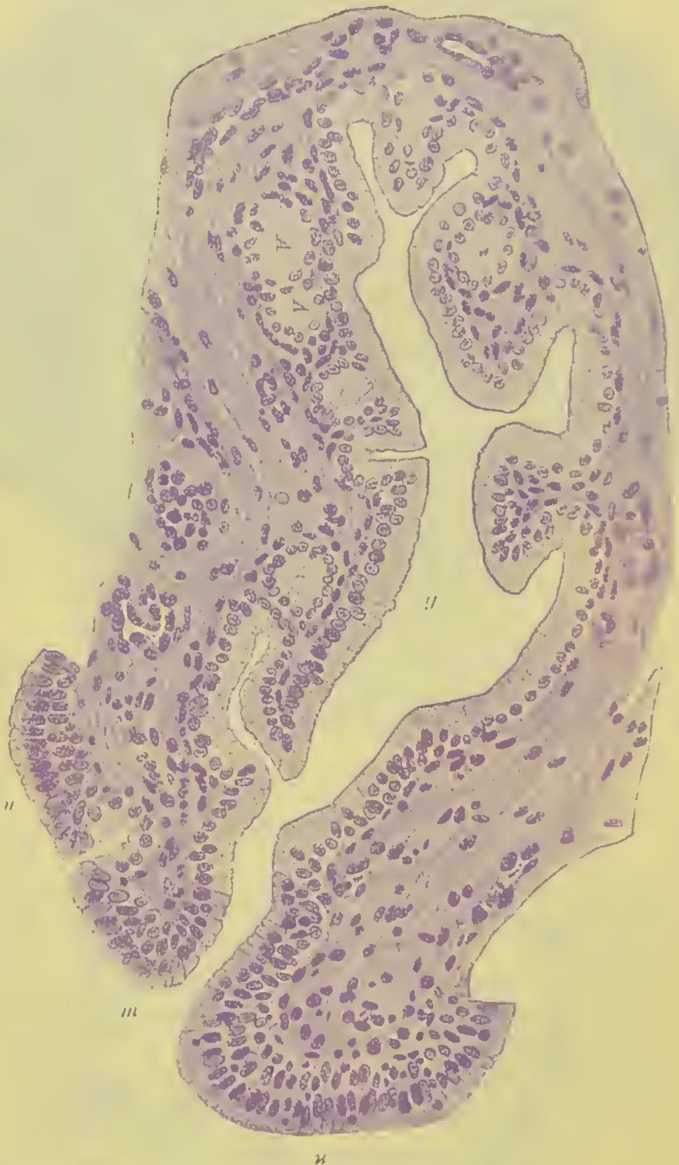

FIG. 481.—SECTION THROUGH THE OPENING OF THE DUCT OF A GLAND INTO THE MALE URETHRA. (Lichtenberg.)

g, gland; *m*, its mouth; *u*, epithelium of urethra. The gland is similar in structure to Cowper's glands, but simpler in conformation. Its cells are mucus-secreting.

epithelium rests upon a vascular mucous membrane, which contains longitudinally disposed plain muscular fibres, and in the membranous urethra, circularly disposed cross-striated fibres. Outside the mucous membrane is a coating of submucous tissue, with two layers of plain muscular fibre—an inner longitudinal and an outer circular. Outside this again is a close plexus of small veins which is connected with, and may be said to form part of, the corpus spongiosum.

The *mucous membrane* of the urethra is beset with small mucous glands, simple and compound (*glands of Littré*). There are also a number of oblique recesses termed *lacunæ*. Besides these small glands and glandular recesses, two compound racemose glands open into the bulbous portion of the urethra (*Cowper's glands*). Their acini are lined by clear columnar cells which yield a mucus-like secretion (fig. 481).

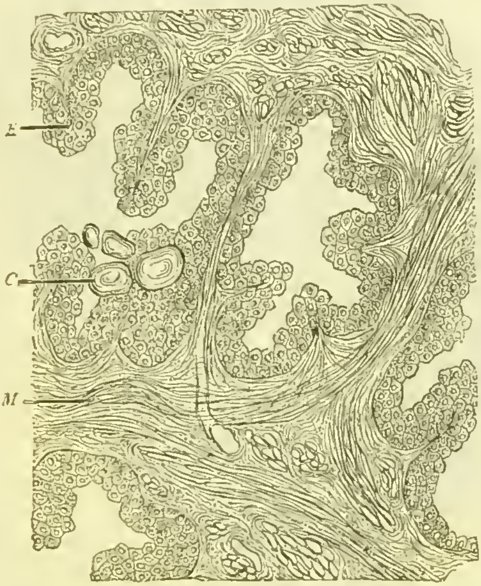

FIG. 482. –SECTION OF PROSTATE. (Heitzmann.)
M, muscular tissue; *E*, epithelium; *C*, concretions.

The **prostate**, which surrounds the commencement of the urethra, is a muscular and glandular mass, the glands of which are composed of tubular alveoli, lined by columnar epithelium, with smaller cells lying between them and the basement-membrane (fig. 482). Their ducts open upon the floor of the urethra. In old subjects the tubules often contain colloid or calcareous concretions. The muscular tissue is of the plain variety.

Blood-vessels and nerves are numerous. The nerves are provided with small ganglia and are distributed partly to the muscular tissue, partly to the glands, and others (sensory) to the capsule, and to the wall of the urethra. The sensory nerves end in plexuses and in peculiar terminal corpuscles like simple Pacinian bodies (Timofeew).

The **testicle** is inclosed by a strong fibrous capsule, the *tunica albuginea* (figs. 483, 484). This is covered externally with a layer of serous epithelium reflected from the *tunica vaginalis*. From its inner surface there proceed fibrous processes or *trabeculæ*, which imperfectly subdivide the organ into lobules, and posteriorly the capsule is prolonged into the interior of the gland in the form of a mass of fibrous tissue, which is known as the *mediastinum testis*. Attached to the posterior margin of the body of the gland is a mass (*epididymis*) which when investigated is found to consist of a single convoluted tube, receiving at its upper end the *efferent ducts* of the testis and prolonged at its lower end into a thick-walled muscular tube, the *vas deferens*, which conducts the secretion to the urethra.

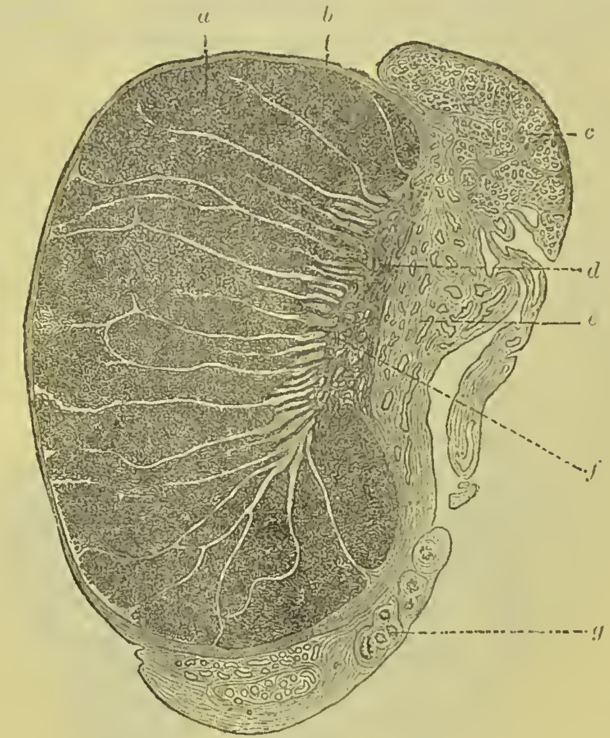

FIG. 483.—SECTION OF HUMAN TESTIS AND EPIDIDYMIS, SOMEWHAT MAGNIFIED. (Böhm and v. Davidoff.)

a, glandular substance divided into lobules by septa of connective tissue; *b*, tunica albuginea; *c*, head of epididymis; *d*, rete testis; *e*, middle part or body of epididymis; *f*, mediastinum giving origin to the septa; *g*, sections of the commencing vas deferens.

The glandular substance of the testicle is wholly made up of *convoluted tubules*, which when unravelled are of very considerable length. Each commences near the tunica albuginea, and after many windings terminates, usually after joining one or two others, in a *straight tubule*, which passes into the mediastinum, and there forms, by uniting with the other straight tubules, a network of intercommunicating vessels of varying size, which is known as the *rete testis* (fig. 485). From the rete a certain number of efferent tubules arise, and after a few convolutions pass into the tube of the epididymis.

The *straight tubules* which lead from the convoluted seminiferous tubes into the rete testis are lined only by a single layer of clear flattened or cubical epithelium. The tubules of the *rete* also have a simple epithelial lining; both in these and in the straight tubules the basement-membrane is absent, the epithelium being supported directly by the connective tissue of the mediastinum.

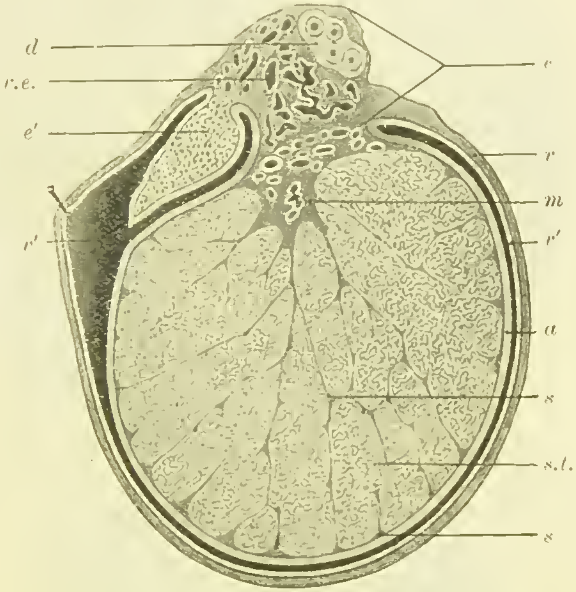

FIG. 484.—TRANSVERSE SECTION OF TESTICLE AND EPIDIDYMIS, MAN. (Eberth.)

a, tunica albuginea; *s.t.*, seminiferous tubules; *s*, trabeculæ dividing the gland into lobules; *v*, tunica vaginalis; *v′*, cavity of tunica vaginalis; *m*, mediastinum testis; *e*, epididymis; *e′*, caput epididymis; *v*, vas deferens (cut four times); *.ve.*, vasa efferentia.

The *efferent tubules* which pass from the rete to the epididymis are lined by columnar ciliated epithelium. In man their lumen is irregular in section, and the inner surface pitted with depressions (intra-epithelial glands) lined by short clear non-ciliated cells (J. Schaffer). The *tube of the epididymis* is lined by long columnar cells having at their bases smaller cubical cells with spherical nuclei (fig. 486). The columnar cells are provided with what appear to be bunches of cilium-like fibrils projecting into the lumen of the tube. These apparent cilia are, however, not vibratile as was formerly supposed, and are therefore not true cilia (Neumann, Myres-Ward). They appear to vary in development in different cells, and are probably connected in some way with the formation of the secretion of the epididymis and its extrusion into the lumen of the tube. The epididymis cells exhibit canaliculi in their cytoplasm, which, according to Holmgren, communicate with the exterior at the attached border of the cell (fig. 487). The tube of the epididymis has a considerable amount of plain muscular tissue in its wall (fig. 486).

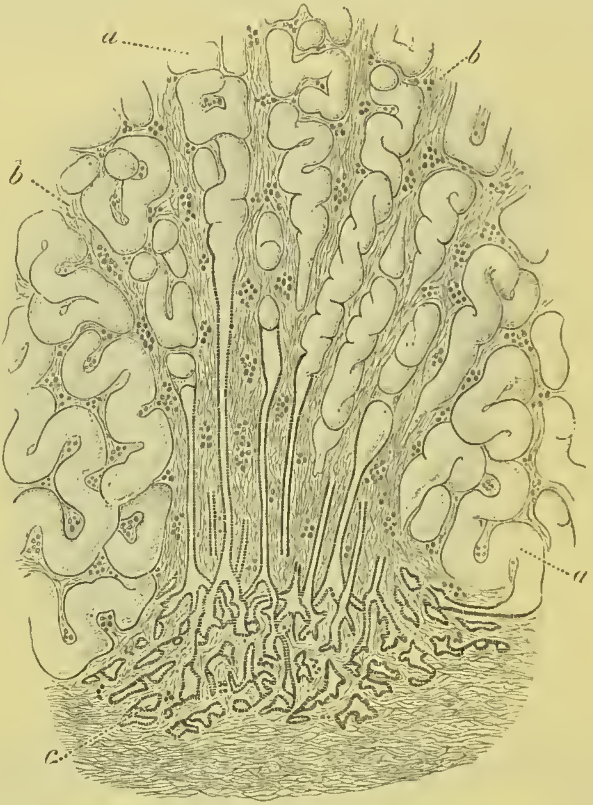

FIG. 485.—PASSAGE OF CONVOLUTED SEMINIFEROUS TUBULES INTO STRAIGHT TUBULES AND OF THESE INTO THE RETE TESTIS. (Mihalkowicz.)

a, seminiferous tubules ; *b*, fibrous stroma continued from the mediastinum testis : *c*, rete testis.

The *vas deferens* (fig. 488) is a thick-walled tube, formed of an outer layer of longitudinal bundles of plain muscular tissue, and within this an equally thick layer of circular bundles of the same tissue ; within this again is a thinner layer of longitudinal muscle. There is a good deal of connective and elastic tissue between the muscular bundles. The tube is lined by a mucous membrane, the inner surface of which is covered by columnar non-ciliated epithelium.

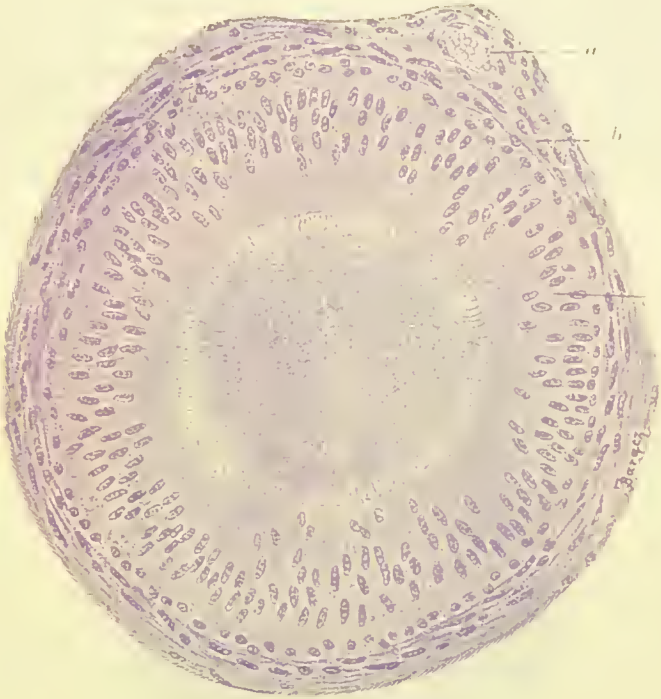

FIG. 486.—SECTION OF THE TUBE OF THE EPIDIDYMIS. (Szymonowicz.) Magnified 300 diameters.

a, blood-vessel ; *b*, circular muscular fibres ; *c*, epithelium.

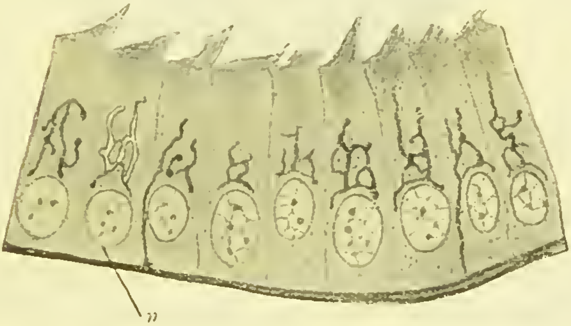

FIG. 487.—CELLS OF EPIDIDYMIS, SHOWING CANALISATION OF THE CYTOPLASM. (E. Holmgren.)

n, nucleus. In two cells the canals extend to the basement membrane.

The *ampullæ* of the vasa deferentia, and the *vesiculæ seminales*, are in structure similar to the vas deferens, but their corrugated walls are much thinner and less muscular.

Intertubular tissue.—The connective tissue between the tubules of the testis is generally of very loose texture, and contains numerous lymphatic clefts, which form an intercommunicating system of commencing lymphatic vessels. Lying in this intertubular tissue are strands of polyhedral epithelium-like cells (*interstitial cells*, see figs. 490, 491) of a yellowish colour; they are much more abundant in some species of animals (cat, boar) than in others. They accompany the blood-vessels before these break up to form the capillary networks which cover the walls of the seminiferous tubules.

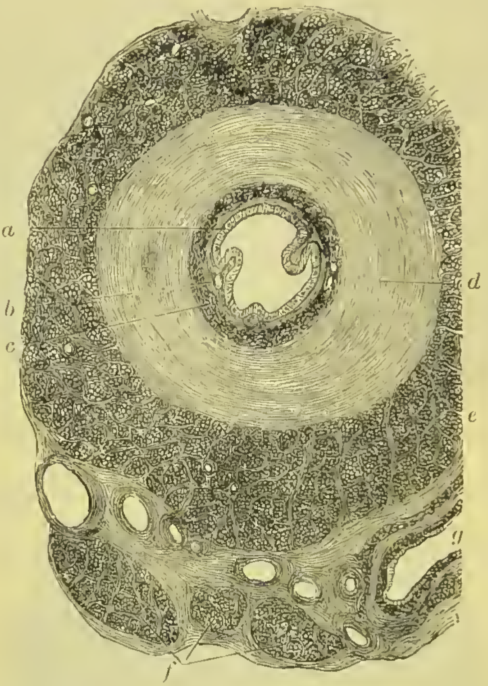

FIG. 488.—SECTION ACROSS THE COMMENCEMENT OF THE VAS DEFERENS. (Klein.)

a, epithelium; *b*, mucous membrane; *c*, *d*, *e*, inner, middle, and outer layers of the muscular coat; *f*, bundles of the internal cremaster muscle; *g*, section of a blood-vessel.

The interstitial cells contain in many animals yellowish-brown fat globules (staining with osmic acid), and also sometimes needle-shaped crystals (proteid). Similar fatty globules may occur in the Sertoli cells of the seminiferous tubules (see above), and have been thought to be derived from those of the interstitial tissue.

Structure of the tubules.—The *seminiferous tubules* are formed of a connective-tissue membrane, which has a lamellar structure. The lamellæ are covered by flattened cells; fibres, chiefly elastic, occupy the substance of the lamella. In the adult the tubules contain several layers of epithelium-cells. But in the testicle of the child there is no clear distinction into layers, the cells being all more or less similar except where they are in process of division (fig. 489). Of these layers, the one next to the basement-membrane is a stratum of clear cubical cells (*spermatogonia* or *spermogons*, figs. 490, 491, *a*), the nuclei of which for the most part exhibit the irregular network which is characteristic of the resting condition, but in certain tubules show indications of division. Here and there between the spermatogonia some of the lining epithelium-cells are enlarged, and project between the more internal layers, being connected with groups of developing spermatozoa. These enlarged cells are the *cells of Sertoli* (fig. 494, *a'*, *a''*; fig. 497).

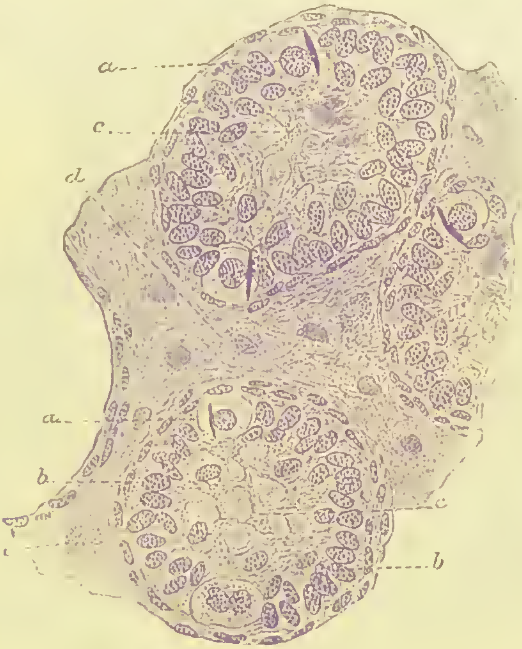

FIG. 489.—SECTION OF A TESTICLE OF A 9-YEAR OLD CHILD. (Spangaro.)

a, enlarged cells (spermatogonia), some of them dividing; several contain crystals (Lubar's crystals); *b*, cells lining the tubule; *c*, coagulated contents of tubule; *d*, interstitial tissue; *e*, mast-cells.

Next to this lining epithelium is a zone of larger cells (*spermatocytes* or *spermocytes*, fig. 494, *b*), the nuclei of which are usually in some stage of hetero- or homo-typical mitotic division; these cells may be two or three deep (as in *a*, fig. 491). Next to them, and most internal, are to be seen in some tubules (fig. 491, *b* and *c*) a large number of small protoplasmic cells with simple spherical nuclei (*spermatids* or *spermids*, fig. 494, *c*). In other tubules the spermatids are elongated, and the nucleus is at one end, and in others again these elongated cells are converted into evident spermatozoa, which lie in groups: their heads projecting between the deeper cells and connected with one of the Sertoli cells of the lining epithelium, and their tails emerging into the lumen of the tubule (fig. 491, *b*). As they become matured they gradually shift altogether towards the lumen, where they eventually become free (*c*). During the time that this crop of spermatozoa has been forming, another set of spermocytes has been produced by the division of the spermogonia, and on the discharge of the spermatozoa the process is repeated as before (see diagram, fig. 494).

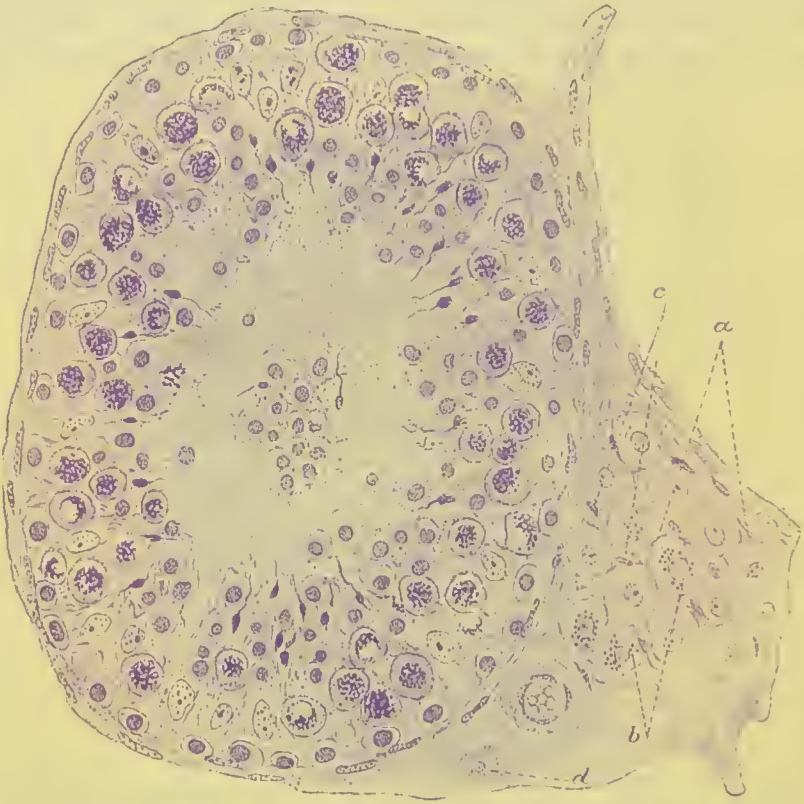

FIG. 490.—SECTION FROM THE TESTICLE OF A 42-YEAR OLD MAN. (Spangaro.)

a, interstitial cells; *b*, some containing pigment; *c*, nuclei of ordinary connective-tissue cells; *d*, mast-cell. In the section of the tubule may be seen in succession from without in, spermatogonia, spermatocytes, spermatids, and spermatozoa. A few spermatids and spermatozoa are detached and occupy the middle of the tubule.

The **spermatozoa.**—Each spermatozoon or sperm consists of three parts, a *head*, a *midde part* or *body*, and a long tapering and vibrating *tail* (fig. 492). In man the head is of a flattened oval shape, somewhat more flattened anteriorly; in some animals it bears a small barb-like projection at its extremity, but this appears to be absent in the human spermatozoon. The apical part is covered by a cap of a somewhat different appearance from the rest—the *head-cap*. The *middle-piece* is in man short and cylindrical, and has a spiral fibre passing round it. An *axial fibre*, itself fibrillated, passes from a knob close to the head right through the body and tail. The *tail* is the longest part of the spermatozoon, and when examined with the microscope in the fresh condition is seen to be in continual vibratile motion, the action resembling that of a cilium. The extremity of the tail (*end-piece*) forms a distinct part of the spermatozoon, and in some animals may split into two or three fibrils; these can also sometimes be traced along the whole length of the tail. Human spermatozoa are about 0·05 mm. ($\frac{1}{500}$ inch) long, the head and middle-piece each measuring about $\frac{1}{10}$th of this amount.

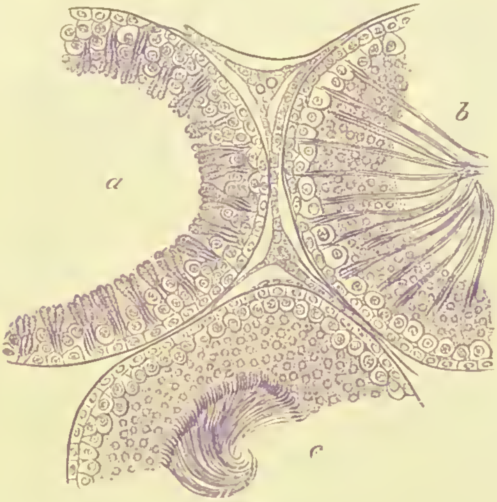

FIG. 491.

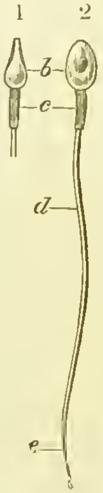

FIG. 492.

FIG. 491.—SECTION OF PARTS OF THREE SEMINIFEROUS TUBULES OF THE RAT.

a, with the spermatozoa least advanced in development; *b*, more advanced; *c*, containing fully developed spermatozoa. Between the tubules are seen strands of interstitial cells with blood-vessels and lymph-spaces.

FIG. 492.—HUMAN SPERMATOZOA. $\frac{1000}{1}$. (G. Retzius.)

1, in profile; 2, viewed on the flat; *b*, head; *c*, middle-piece; *d*, tail; *e*, end-piece of the tail, which is described as a distinct part by Retzius.

In different animals the shape of the head and the extent of middle-piece and tail vary greatly (fig. 493). In the rat (fig. 495, 7) the head is long, and is recurved anteriorly; it is set obliquely on the middle-piece, which is also of considerable extent, and which has a closely wound spiral filament encircling it (H. H. Brown). In the newt the head is long and tapering, and the tail has a membranous expansion, attached in a spiral manner along its whole length. This has also been described in the human spermatozoon, but its existence here is doubtful. In decapods, which possess no cilia, the spermatozoa are stellate and motionless (fig. 493, *l*); in nematoid worms they are amœboid (fig. 493, *k*). Sometimes two distinct kinds of spermatozoa are met with in the same species of animal, one kind being far the larger in size (giant spermatozoa) but much less numerous. Such giant spermatozoa have been observed in man.

Although the tail of the spermatozoon is usually classed with cilia, it exhibits far greater complexity of structure and is a much more highly differentiated structure. Spermatozoa also differ from cilia in being highly resistant to putrefaction and to chemical reagents, even including the strongest acids and alkalies.

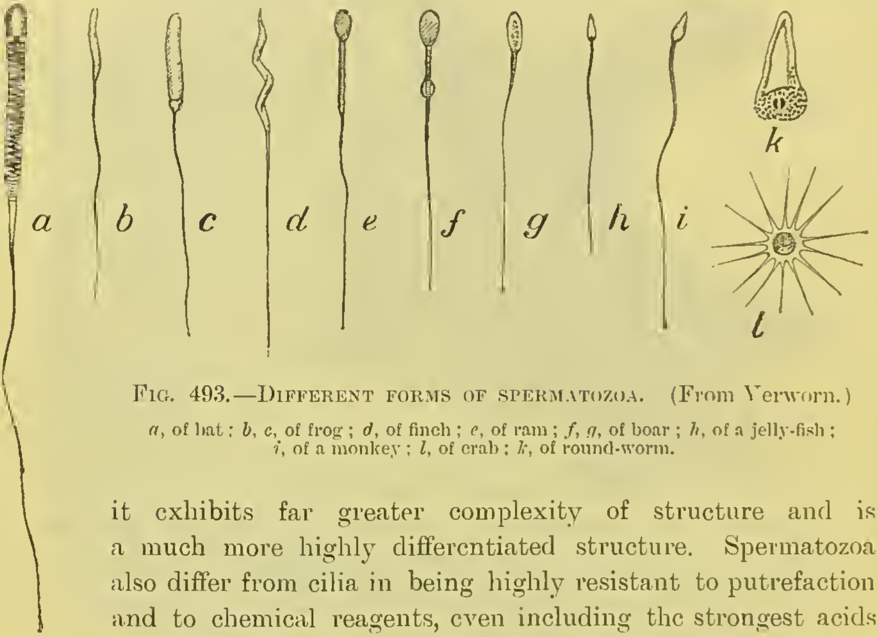

Fig. 493.—Different forms of spermatozoa. (From Verworn.)

a, of bat; *b*, *c*, of frog; *d*, of finch; *e*, of ram; *f*, *g*, of boar; *h*, of a jelly-fish; *i*, of a monkey; *l*, of crab; *k*, of round-worm.

Spermogenesis.—The spermatozoa are developed from the small cells (spermatids) which form the innermost stratum of the seminal epithelium, and these are themselves produced by the division of the large spermocytes of the second layer. It is probable that fresh spermocytes are formed by division of some of the lining epithelium-cells or spermogons. The cycle of changes therefore which takes place is as follows: 1. Division of a lining epithelium-cell or spermogon into two, one of which grows larger ("growing cells" of H. H. Brown), becomes a spermocyte, and passes into the second layer, while the other remains in the first layer. 2. Division of the spermocyte. 3. Further division of the daughter-spermocytes thus produced. The four cells (spermatids) which result from this double division possess only one-half the somatic number of chromosomes in their nuclei.

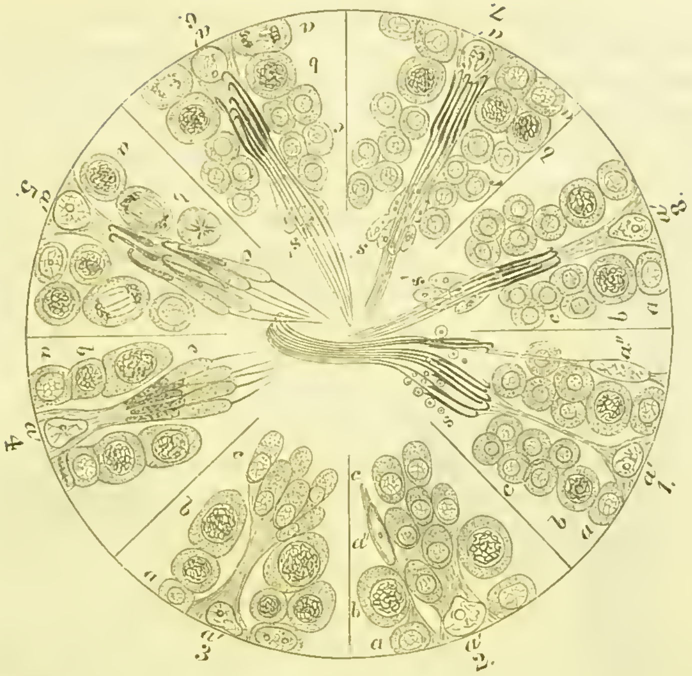

FIG. 494.—DIAGRAM EXHIBITING THE CYCLE OF PHASES OF SPERMOGENESIS (RAT).

a, lining epithelium-cells or spermatogonia, seen dividing in 6; *a′*, *a″*, Sertoli cells; *b*, spermatocytes, with skein-like nuclear filaments. These cells are seen actively dividing in 5. *c*, spermatids, forming an irregular column or clump in 6, 7, 8, and 1, and connected to an enlarged Sertoli cell, *a′*, of the lining epithelium in 2, 3, 4, and 5. In 6, 7, and 8 advanced spermatozoa of one crop are seen between columns of spermatids of the next crop. *s′*, parts of the spermatids which disappear when the spermatozoa are fully formed; *s*, seminal granules.

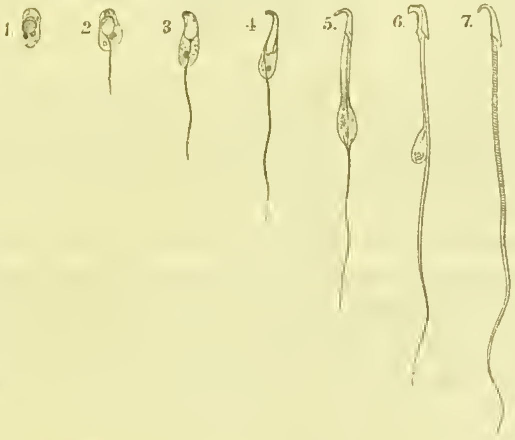

FIG. 495.—SPERMATOZOA FROM THE RAT IN DIFFERENT STAGES OF DEVELOPMENT. (H. H. Brown.)

1-6, developing spermatozoa from the testicles; 7, a mature spermatozoon from the vas deferens. The remains of the protoplasm of the cell, which is seen in 6, still adhering to the middle-piece of the spermatozoon and containing a number of chromatin granules, appears to be thrown off as the spermatozoon matures.

"reduction" having been effected in the final cell-divisions by which the spermatids are produced (see p. 17). 4. Elongation of the spermatids and their gradual conversion into spermatozoa. As they undergo this conversion their grouping becomes more evident, and each group is found to be connected with a cell of Sertoli (figs. 494, *a′*, 497), which probably ministers to their nutrition. This cell undergoes a gradual process of elongation, so that the spermatozoa by the time they are fully developed are brought to the lumen of the tube, in which they then become free. In the meantime other alternate groups of spermatids from which the next crop of spermatozoa will be derived are being formed in the same manner, passing through the same cycle of changes. So that in a longitudinal section even of the same tubule different phases of development may be observed, and in different tubules of the same testicle every phase may be traced. The accompanying diagram (fig. 494), which is constructed from drawings by H. H. Brown, illustrates the cycle of changes above described; it is divided into eight parts, each of which shows the condition of the epithelium of a seminiferous tubule at a particular stage.

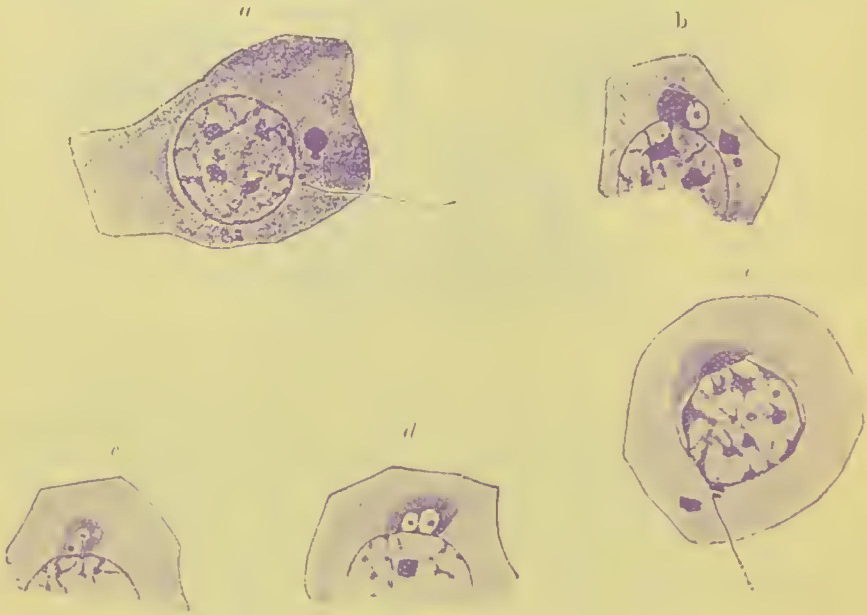

FIG. 496.—CHANGES IN THE SPERMATIDS IN THE COURSE OF FORMATION OF THE SPERMATOZOA. (Niessing.)

The tail filament is seen (in *a* and *e*) to extend from the centrosome, which lies close to the nucleus. The head-cap (shown in *e*) is produced by a transformation of part of the archoplasm which becomes vacuolated (*b*, *c*, *d*).

Each spermatid becomes converted into a spermatozoon in the following manner (figs. 495, 496). The nucleus forms the chief part of the head, while the tail develops as an outgrowth of the centrosome and cytoplasm. The tail-filament appears within the protoplasm, growing out from the centriole of the cell, which lies close to the nucleus (fig. 496). The centriole is double, and one of its two particles forms an annular expansion or ring which, as development proceeds, moves down the tail-filament until it reaches the place where this leaves the cytoplasm: here it ultimately forms the limit of the body or middle-piece of the spermatozoon. The archoplasm (see p. 9) assists in forming the head of the spermatozoon; a portion (the *idiozome* of Meves) at an early stage separates from the rest, lying apically to the nucleus. Within this portion vacuoles form (fig. 496, *b*, *c*, *d*) which presently run together into a clear non-stainable globule which flattens out over the nucleus and forms (fig. 496, *e*) the head cap of the spermatozoon; as development proceeds this may become indistinguishable from the rest of the head. The spiral fibre of the middle-piece is developed from mitochondria in the spermatid (Benda) (fig. 7, p. 6).

A portion of the protoplasm of each spermatid containing a number of chromatin-particles (seminal granules) becomes detached and disintegrated before the spermatozoon is fully matured (fig. 494, *s*, *s'*).

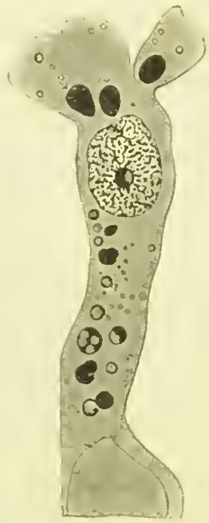

FIG. 497.—A CELL OF SERTOLI WITH WHICH THE SPERMATIDS (THREE OF WHICH ARE SHOWN) ARE BEGINNING TO BE CONNECTED: HUMAN. (Bramman.)

The cell contains globules (of nutritive substance) staining with osmic acid, and similar but smaller globules are also seen in the spermatids. The "ring" formed around the tail filament by one of the particles of the centrosome (see text) is shown in each of these spermatids close to the "head."

A few spermocytes undergo incomplete division, and the resulting spermatids are large (giant spermatids) and contain either one large nucleus or two or more nuclei which ultimately blend to form the head of the spermatozoon. In these cases there are a corresponding number of centrosomes, from each of which a tail-filament may become developed.

LESSON XXXVIII.

GENERATIVE ORGANS OF THE FEMALE.

1. Sections of the ovary of the non-pregnant rabbit or cat. (If from a pregnant animal the organ may be largely occupied by luteal tissue.) Study the sections with a low power, observing the small and large Graafian follicles, each inclosing an ovum, scattered through the stroma. Measure some Graafian follicles of different sizes; make a general sketch of a section under the low power. Then sketch carefully two or more of the follicles with their contents under a high power.

2. Section across the Fallopian tube. Sketch a section under the low power.

3. Section across the body of the uterus, or across a cornu of a bicorned uterus. Observe with the naked eye the thickness of the muscular and mucous coats respectively. Notice the (ciliated) columnar epithelium lining the organ and extending into the glands of the mucous membrane. Draw a part of a section under the low power.

4. Section of the placenta. Notice the venous spaces occupied by blood-corpuscles, and within the spaces sections of the fœtal villi.

5. Sections of the mucous membrane of the vagina. Notice the stratified scaly epithelium which lines it and which is continued over the projecting part of the os uteri.

6. Take the fresh ovary of a recently killed animal and with a needle or fine scalpel-point prick one of the largest and most prominent of the Graafian follicles. The organ must be held just over a slide so that on pricking the follicle the fluid contents may spurt out on to the glass. Examine the drop of liquor folliculi with a low power for the escaped ovum, which will be surrounded by follicular cells. When found place a piece of hair in the drop, cover with cover-glass and examine with high power.

THE OVARY.

The **ovary** is a small solid organ, composed of a *stroma* of fibrous tissue, with many spindle-shaped cells, and also containing, near its attachment to the broad ligament, a large number of plain muscular fibres. It is covered by a layer of small columnar epithelium-cells (*germinal epithelium*, fig. 499, *a*), between which may here and there be seen a few larger spheroidal cells, with large round nuclei. In the young subject the epithelium occasionally dips down into the subjacent stroma.

The stroma is beset with vesicles of different sizes, the smallest being near the surface of the organ, the larger ones placed more deeply in the stroma, although, as they increase in size, they extend towards the surface (fig. 498).

These vesicles are the *Graafian follicles.* Each Graafian follicle has a proper wall (*theca folliculi*) formed of a layer derived from the stroma, and a special inner layer containing large cells: both are highly vascular. Each follicle contains an *ovum* and *epithelium.* In the smallest follicles the ovum is small, and the epithelium of the follicle is formed of a single layer of cells which may be flattened against the ovum (fig. 500). In somewhat larger follicles the epithelium-cells are in two layers, and these are columnar in shape (fig. 502, E). In still larger ones, each of these two layers is formed of several strata of cells, and fluid has begun to collect between the layers at one part. Of the two layers, the one which lines the cavity of the follicle is termed the *membrana granulosa*, while the mass of cells which more immediately surrounds the ovum is known as the *cumulus* or *discus proligerus.*

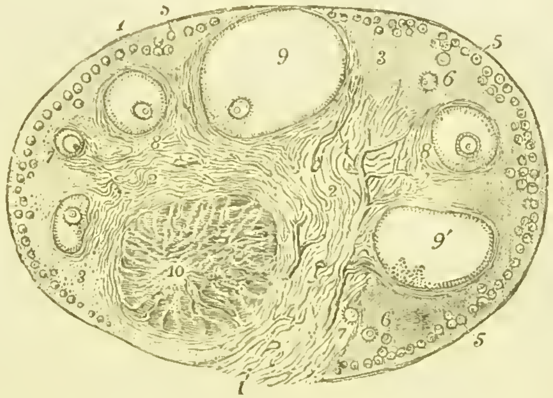

FIG. 498.—SECTION OF THE OVARY OF THE CAT. $\frac{6}{1}$. (Schron.)

1, outer covering and free border of the ovary; *1′*, attached border; *2*, the central ovarian stroma, showing a fibrous and vascular structure; *3*, peripheral stroma; *4*, blood-vessels; *5*, Graafian follicles in their earliest stages lying near the surface; *6*, *7*, *8*, more advanced follicles which are embedded more deeply in the stroma; *9*, an almost mature follicle containing the ovum in its deepest part; *9′*, a follicle from which the ovum has fallen out in preparing the section; *10*, corpus luteum.

In the largest follicles the fluid has much increased in amount, so that the follicle has become gradually larger and more tense. Finally it reaches the surface of the ovary, and projects from the surface, where it eventually bursts, and the liquor folliculi, with its contained ovum, is set free. This event is believed to occur usually at some time during menstruation.

Some of the Graafian follicles do not burst, but, after attaining a certain stage of maturity, undergo a process of retrograde metamorphosis and eventually disappear.

The ovarian ova or oocytes are large spherical cells (fig. 503), about 0·2 mm. ($\frac{1}{125}$ inch) in diameter. When fully formed, as in the largest Graafian follicles, each ovum is surrounded by a thick trans-

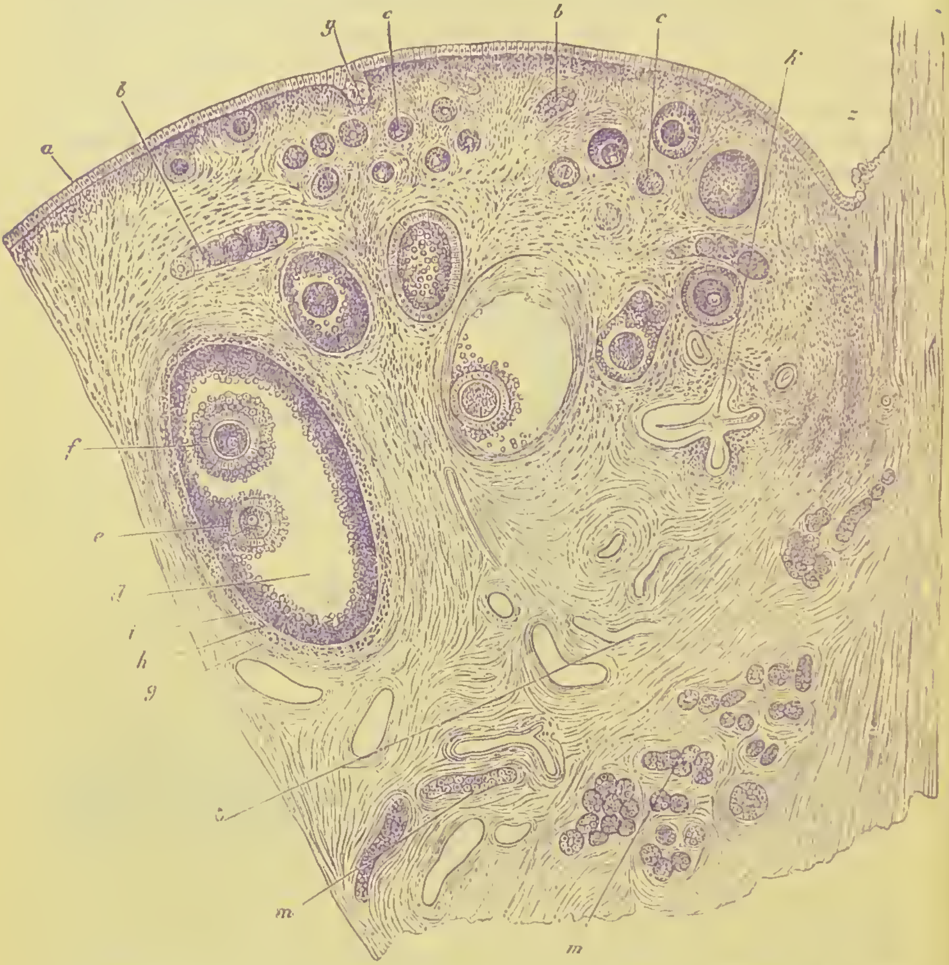

FIG. 499.—SECTION OF THE OVARY OF AN ADULT BITCH. (Waldeyer.)

a, germ-epithelium; *b*, remains of egg-tubes; *c*, small follicles; *d*, more advanced follicle; *e*, discus proligerus and ovum; *f*, second ovum in the same follicle (this occurs but rarely); *g*, outer tunic of the follicle; *h*, inner tunic; *i*, membrana granulosa; *k*, collapsed retrograded follicle; *l*, blood-vessels; *m*, *m*, longitudinal and transverse sections of tubes of the parovarium; *y*, involuted portion of the germ-epithelium of the surface; *z*, place of the transition from peritoneal to germinal or ovarian epithelium.

parent membrane (*zona pellucida*). Within this is the protoplasm of the oocyte (*vitellus*), filled with fatty and albuminous granules (yolk granules). Lying in the vitellus, generally eccentrically, is the large clear round nucleus (*germinal vesicle*), which may show an intranuclear network, and invariably has a well-marked nucleolus (*germinal spot*), sometimes more than one.

Oogenesis.—Both the ova and the epithelium of the Graafian follicles originate from the germinal epithelium of the embryo. This forms at first a simple layer covering the stroma, but later becomes thickened and multiple. After a time rounded cords of epithelium-cells (*egg-tubes* of Pflüger; fig. 502, A) grow down into the stroma, whilst this

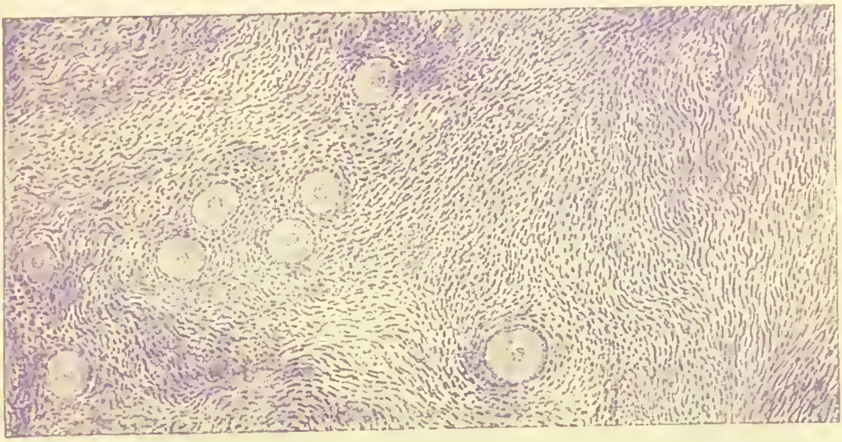

FIG. 500.—SECTION OF PART OF HUMAN OVARY SHOWING SMALL GRAAFIAN FOLLICLES IMBEDDED IN A FIBRO-CELLULAR STROMA. (Sellheim.)

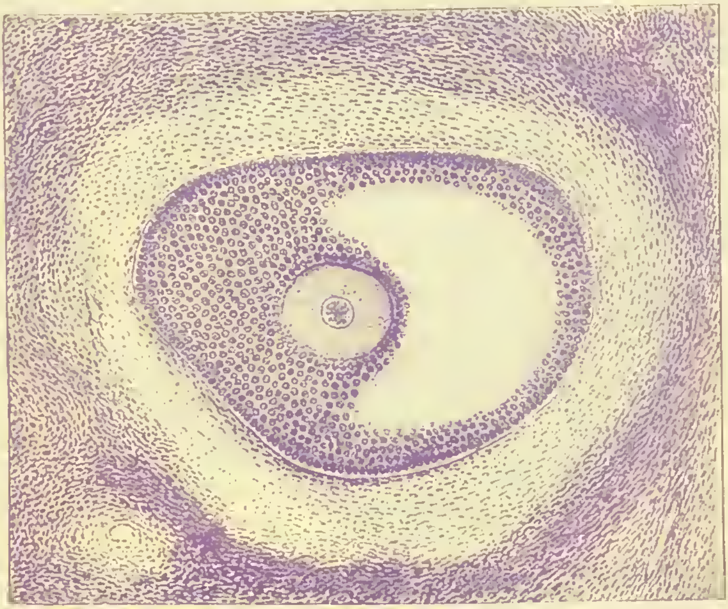

FIG. 501.—A MODERATELY LARGE GRAAFIAN FOLLICLE FROM THE HUMAN OVARY, SHOWING OVUM SURROUNDED BY "DISCUS PROLIGERUS" AND WALL OF FOLLICLE LINED BY "MEMBRANA GRANULOSA." BETWEEN THEM IS AN ACCUMULATION OF LIQUOR FOLLICULI. (Sellheim.)

at the same time grows into the epithelium. The cords presently become broken up by ingrowths of stroma into small isolated nests of epithelium-cells, each of which may represent a Graafian follicle. To form the ova, some of the cells become enlarged (primitive ova), and usually there is one such enlarged cell in each of the isolated

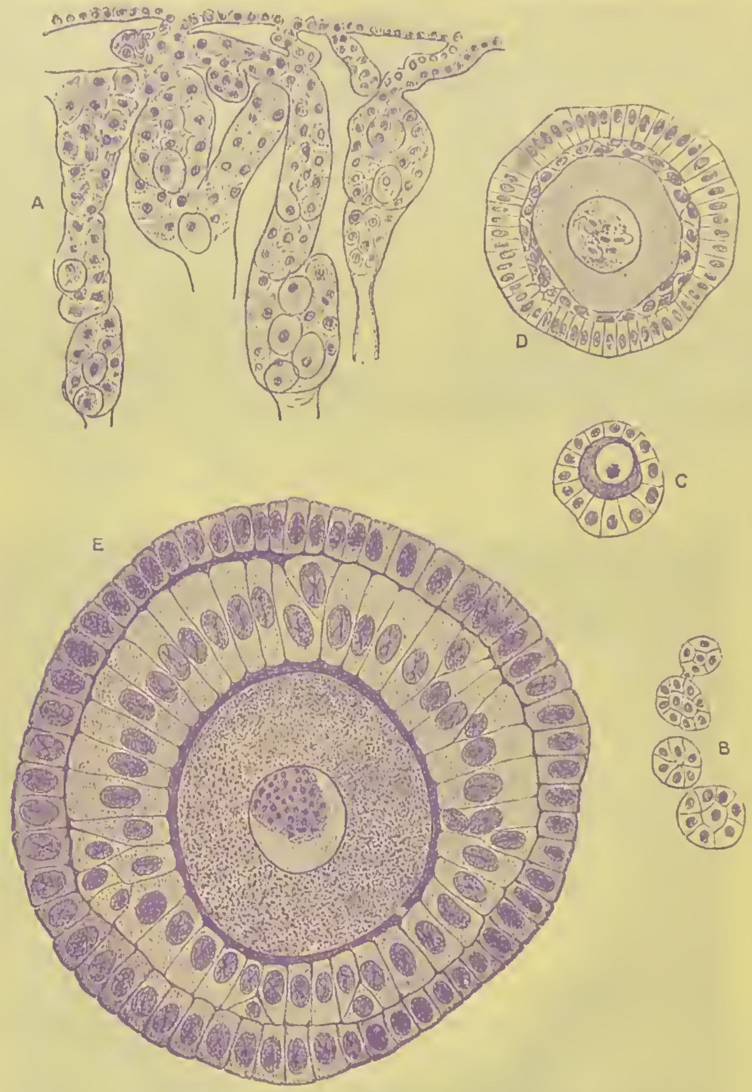

FIG. 502.—FIGURES SHOWING VARIOUS STAGES IN THE DEVELOPMENT OF THE GRAAFIAN FOLLICLES OF THE RABBIT.

A, from ovary of young rabbit, showing "egg-tubes" of Pflüger growing in from germinal epithelium; some of the tubes contain primitive ova; B, primitive Graafian follicles formed from the breaking up of an egg-tube; C, a young Graafian follicle, with a single layer of follicle-epithelium; D, a somewhat older follicle, with the second layer forming within the first; E, a more advanced follicle, showing two complete layers of columnar epithelium surrounding the ovum within the follicle.

nests. The remaining cells form the epithelium of the follicle (see fig. 502, B, C). It is stated that the protoplasm of the ovum remains connected with the cells of the discus proligerus by fine processes which pass through pores in the zona pellucida, and on the other hand, the epithelium-cells of the follicle are themselves inter-connected by protoplasmic bridges, so that the whole forms a kind of syncytium.

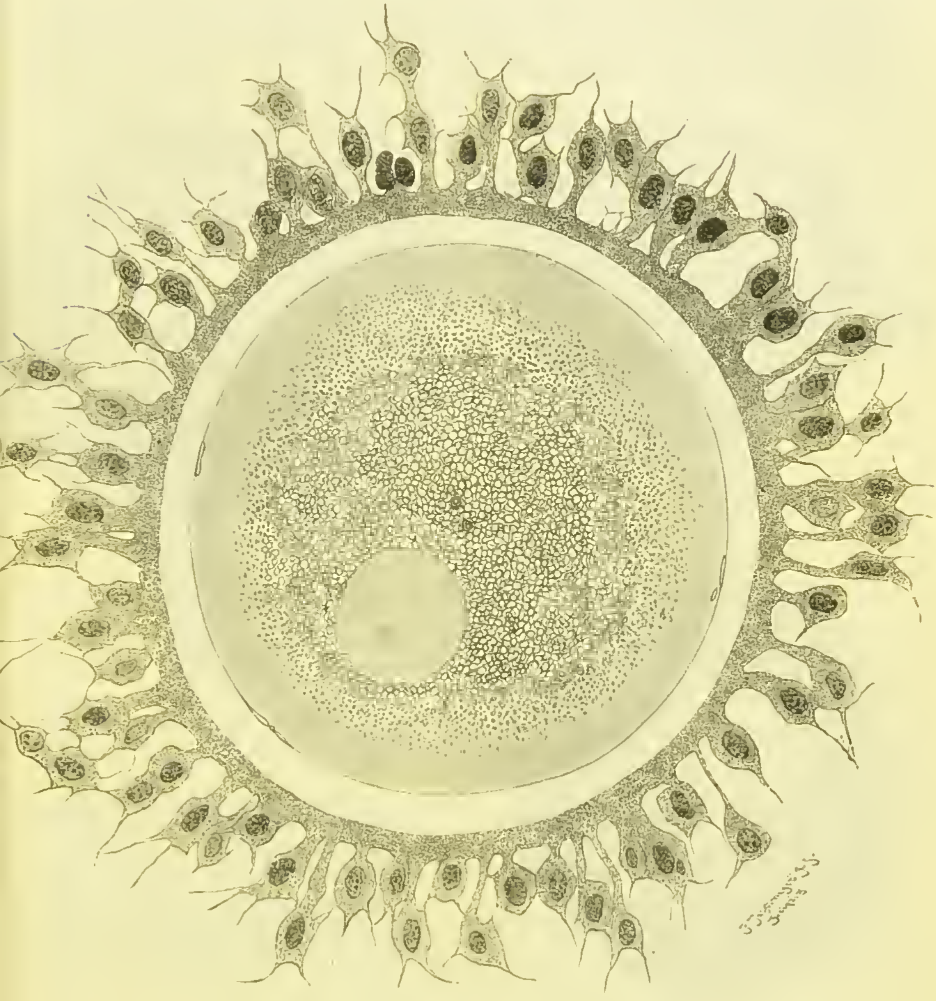

FIG. 503.—HUMAN OVUM; HIGHLY MAGNIFIED. (Waldeyer.)
The zona pellucida is surrounded by cells of the discus proligerus, which are adherent to it.

The *stroma* of the ovary contains, besides the spindle-shaped connective-tissue cells and plain muscular fibres already mentioned, a number of epithelium-like *interstitial cells.* Some of these are derived from the germinal epithelium, and appear capable of developing into ova and follicle epithelium-cells (Lane-Claypon); others have originated from cells of *corpora lutea.* These last are large yellow nodules which are developed out of the Graafian follicles after the ova have been extruded (figs. 504, 505). They consist of columns of large yellowish cells (*luteal cells*), with intervening trabeculæ of vascular fibrous tissue, which converge to a central strand of connective tissue occupying the axis of the nodule (fig. 505). The columns of cells are not unlike those of the cortex of the suprarenal capsule. The corpus luteum is derived from the wall—probably in the main from the epithelium—of the follicle, which becomes thickened and folded by multiplication and hypertrophy of its cells; between the folds connective tissue and blood-vessels grow in from the theca towards the centre of the follicle; in this way the columnar arrangement above mentioned is produced. After persisting for a time the corpus

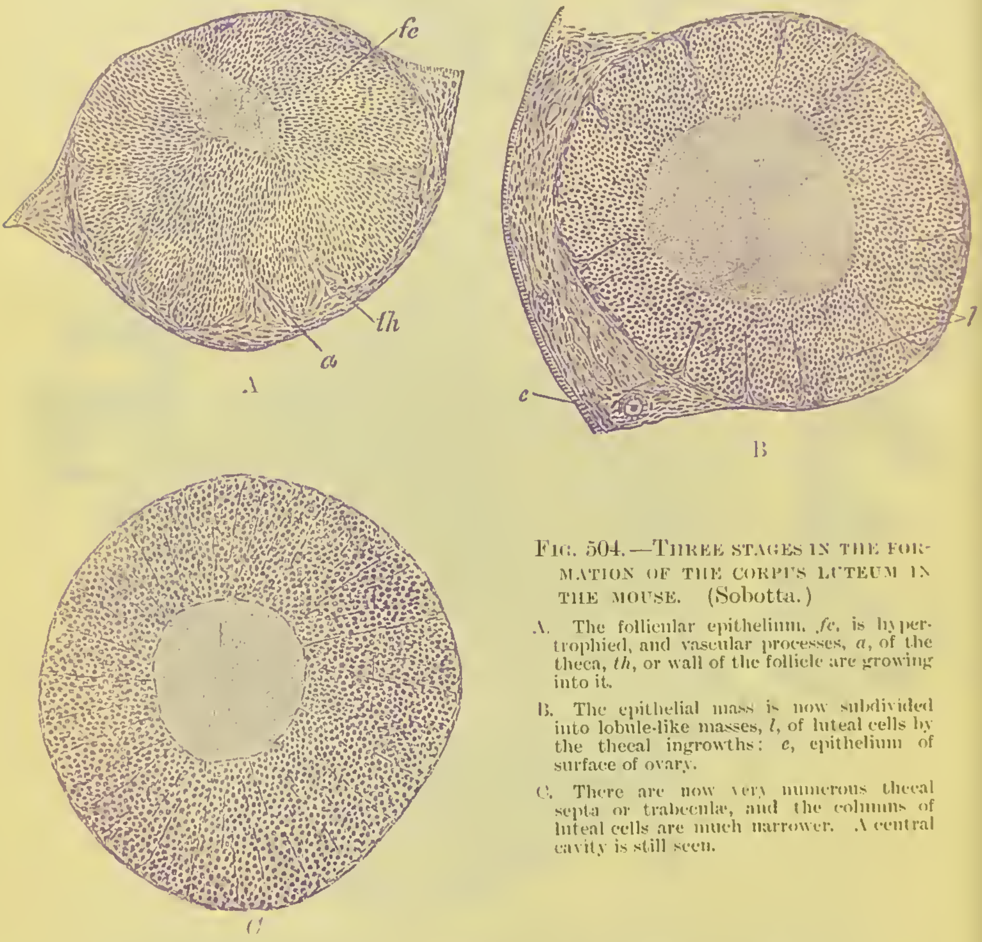

FIG. 504.—THREE STAGES IN THE FORMATION OF THE CORPUS LUTEUM IN THE MOUSE. (Sobotta.)

A. The follicular epithelium, *fc*, is hypertrophied, and vascular processes, *a*, of the theca, *th*, or wall of the follicle are growing into it.

B. The epithelial mass is now subdivided into lobule-like masses, *l*, of luteal cells by the thecal ingrowths: *c*, epithelium of surface of ovary.

C. There are now very numerous thecal septa or trabeculæ, and the columns of luteal cells are much narrower. A central cavity is still seen.

luteum gradually disappears, its tissue becoming merged in the surrounding stroma. Corpora lutea grow much larger and remain much longer persistent in the event of pregnancy supervening.

The use of the corpus luteum is not known certainly, but it has been suggested that it may yield an internal secretion, the effect of which is to produce the fixation of the fertilised ovum in the uterine mucous membrane (Born). In confirmation of this, experiments seem to indicate that gestation does not supervene in animals whose corpora lutea have been destroyed (Fraenkel and Cohn), or from which the ovaries have been removed during the first stages of pregnancy (Marshall and Jolly).

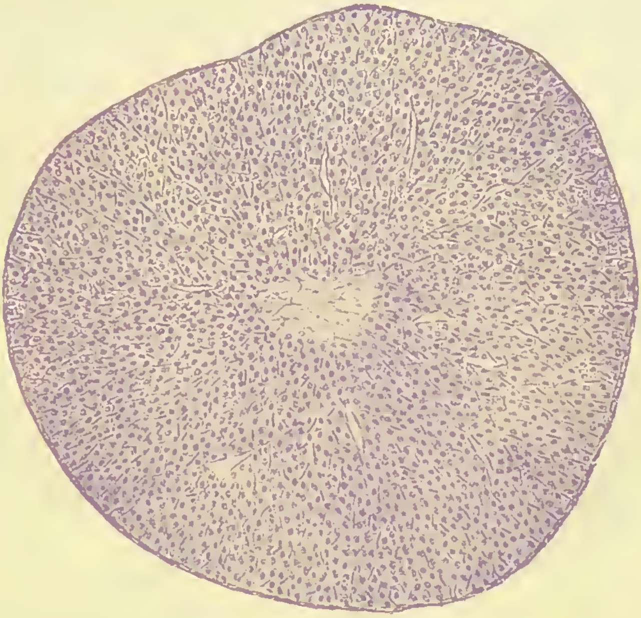

FIG. 505.—CORPUS LUTEUM OF MOUSE. (Sobotta.)

This figure shows a more advanced stage of development, the luteal tissue being now vascularised and the central cavity obliterated.

The blood-vessels of the ovary are very large and numerous, and are especially distributed to the walls of the Graafian follicles, over which they form a close network.

THE FALLOPIAN TUBES AND UTERUS.

The **Fallopian tubes** are lined by a very vascular mucous membrane which is covered with ciliated epithelium, and has numerous longitudinal folds (fig. 506). Externally they are covered by a serous coat, within which is a thin longitudinal stratum of plain muscular fibres overlying circular fibres of the same tissue, but these layers are not distinctly marked off from one another.

The **human uterus** is composed of two parts, the body and cervix. The body of the uterus is formed of the following layers:

1. A *serous layer*, derived from the peritoneum, which covers the greater part of the fundus.

2. A *muscular layer*, which is of considerable thickness and is formed of plain muscular fibres disposed in three, more or less blended, strata. Of these the outer has its fibres arranged partly longitudinally, partly circularly. The middle muscular layer, on the other hand, is thick; its fibres run in different directions, and it contains the ramifications of the larger blood-vessels. The inner layer, again, is thinner and has both longitudinal and circular fibres, many of the latter being prolonged internally into the deeper part of the mucous membrane: the extremities of the uterine glands extend between and amongst its fibres.

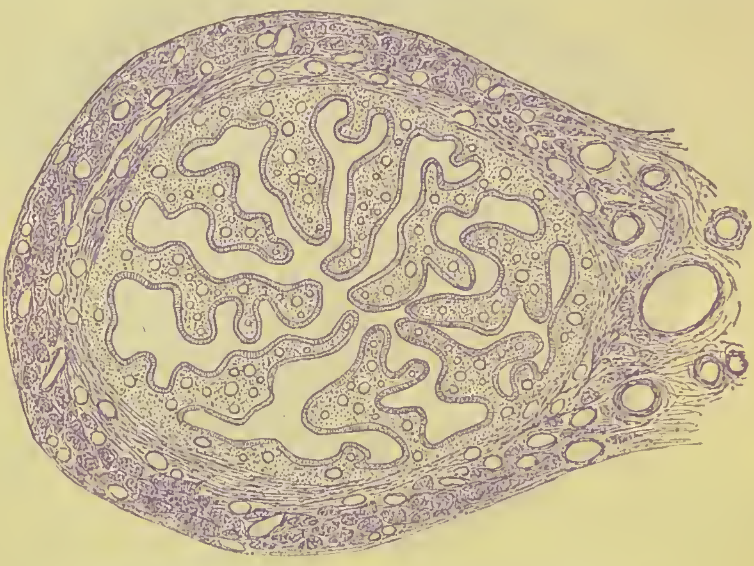

FIG. 506.—SECTION ACROSS THE FALLOPIAN TUBE. (Diagrammatic.)

3. A *mucous membrane*, which is very thick and is composed of soft connective tissue containing a large number of spindle-shaped cells. It is lined by ciliated epithelium and contains long, simple, tubular glands, which take a curved or convoluted course in passing through the membrane (fig. 508). Their (ciliated) epithelium is continuous with that which covers the inner surface of the mucous membrane. In the cervix the mucous membrane is marked by longitudinal and oblique ridges, and the glands are shorter but more complex than those of the body of the uterus, and are lined by columnar mucus-secreting cells. Near the os uteri the epithelium becomes non-ciliated columnar,

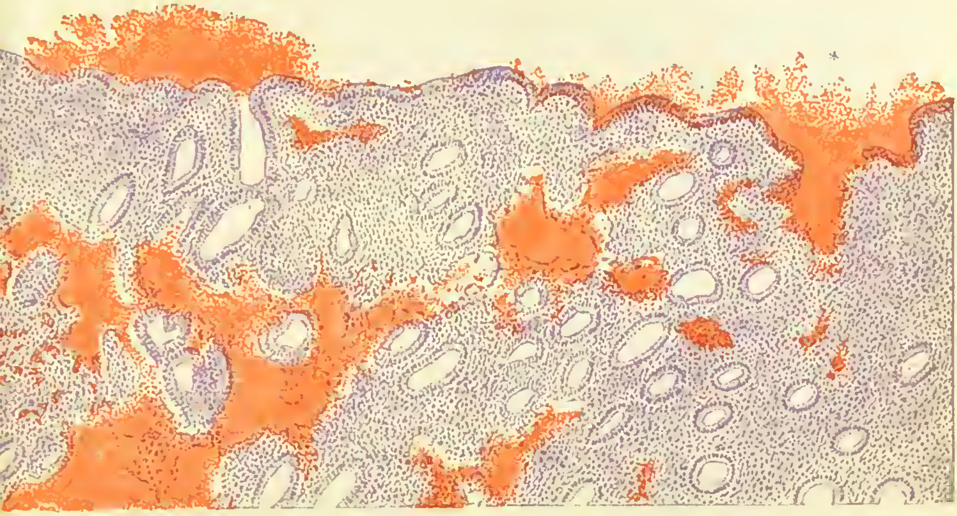

FIG. 507.—SECTION OF MUCOUS MEMBRANE OF HUMAN UTERUS DURING MENSTRUATION, SHOWING MASSES OF BLOOD WHICH HAS ESCAPED FROM RUPTURED CAPILLARIES INTO THE INTERGLANDULAR TISSUE, AND HAS AT ONE PLACE (*) BROKEN THROUGH THE SURFACE EPITHELIUM. (Sellheim.)

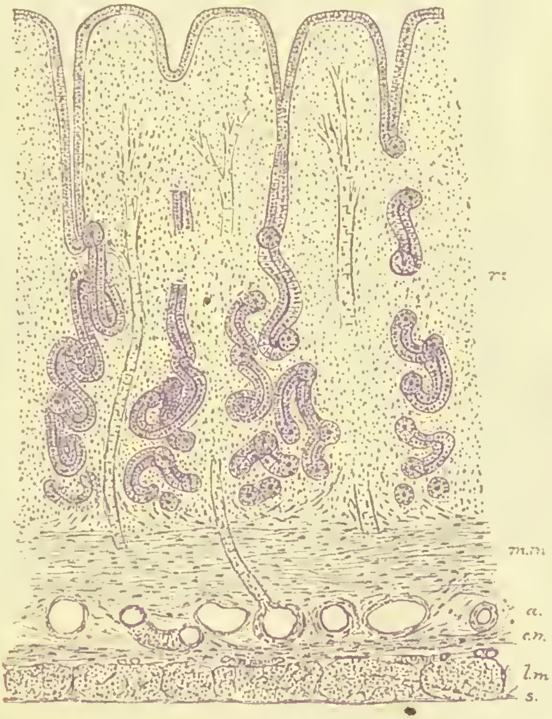

FIG. 508.—SECTION OF A CORNU OF THE RABBIT'S UTERUS.

s, serous layer; *l.m.*, longitudinal muscular fibres; *c.m.*, circular muscular fibres of the muscular coat; *a*, areolar tissue with large blood-vessels; *m.m.*, muscularis mucosæ; *m*, mucous membrane.

and at the margin of the os uteri this passes into a stratified epithelium which overlies vascular papillæ of the corium. The mucous membrane is very vascular, and it also contains a large number of lymph-vessels.

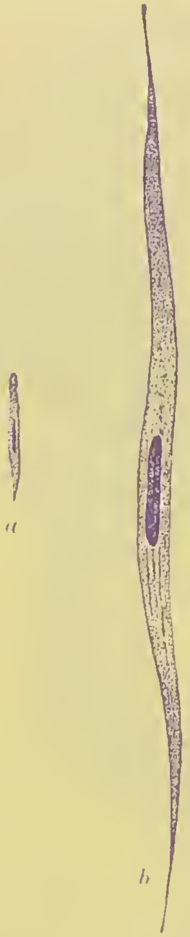

FIG. 509. — MUSCULAR FIBRES (*a*) FROM NON-PREGNANT, (*b*) FROM PREGNANT UTERUS, DRAWN TO THE SAME SCALE. (Sellheim.)

In many animals the uterus is composed of two long tubes (cornua uteri): the arrangement of the muscular tissue in these is simpler than in the human uterus, which has been formed by the fusion of two such tubes. Fig. 508 exhibits the structure of a cornu of the uterus of the rabbit.

At each menstrual period the mucous membrane of the uterus undergoes a partial process of disintegration accompanied by an escape of blood from the capillaries of the membrane (fig. 507). This is succeeded by a rapid renewal of the disintegrated part. Should pregnancy supervene, the process of renewal results in the formation over certain parts of a greatly thickened mucous membrane, with long convoluted glands, which is then known as the *decidua*. The muscular layer also becomes enormously hypertrophied, this hypertrophy being produced by the enlargement of the individual muscle cells (fig. 509).

Structure of the placenta. — When the developing ovum reaches the uterus it becomes imbedded in the thickened mucous membrane (decidua), and processes (fœtal villi), formed at first entirely of epithelial cells, partly distinct, partly conjoined into a syncytium, grow out into the decidua from the chorion which forms the external covering of the ovum (fig. 510). Later vascular mesoderm from the chorion penetrates everywhere into the villi bringing blood from the umbilical vessels. In the meantime large blood sinuses become formed in the decidua, and into these the maternal blood is poured by small spiral arteries, and is taken away by corresponding veins. The fœtal villi are therefore bathed in maternal arterial blood within the sinuses of the decidua (fig. 511), into which for the most part they hang free, although some are attached to the wall of the decidua and others

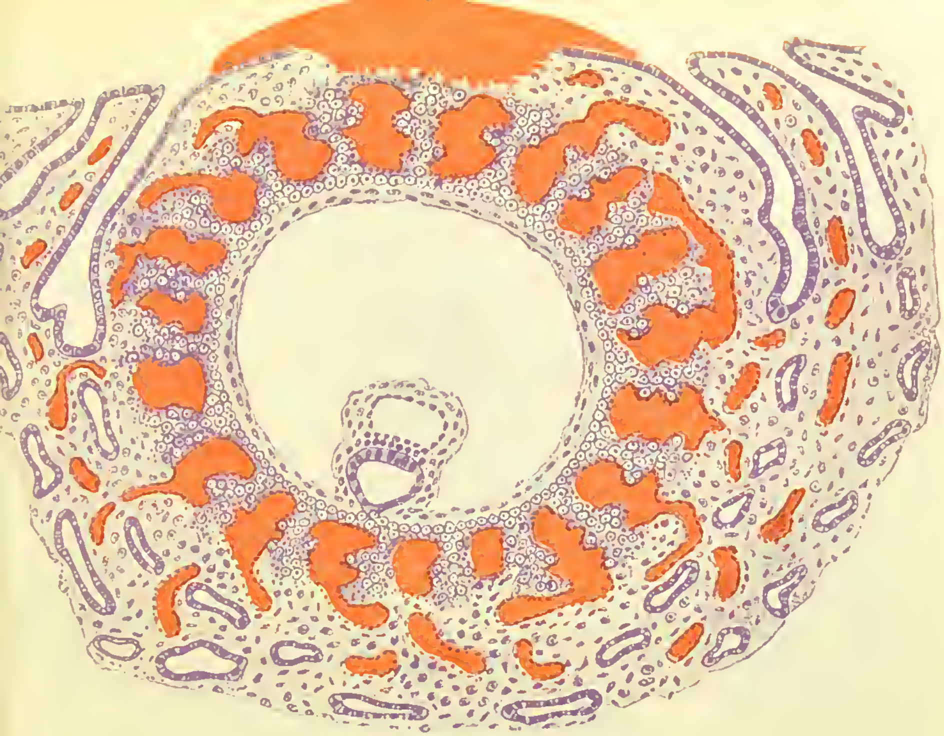

FIG. 510.—DIAGRAM TO ILLUSTRATE THE IMBEDDING OF THE OVUM IN THE DECIDUA AND THE FIRST FORMATION OF THE FŒTAL VILLI IN THE FORM OF A SYNCYTIAL TROPHOBLAST (DERIVED FROM THE OUTER LAYER OF THE OVUM) WHICH IS INVADING SINUS-LIKE BLOOD-SPACES IN THE DECIDUA. (T. H. Bryce.)

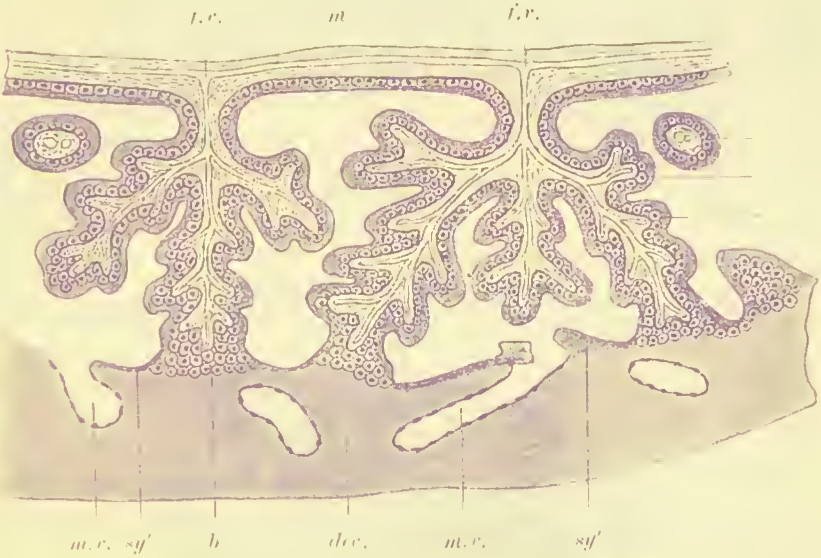

FIG. 511.—DIAGRAM OF A FURTHER STAGE IN THE FORMATION OF THE PLACENTA, SHOWING THE FŒTAL VILLI WITHIN THE BLOOD-SPACES OF THE PLACENTA AND PARTLY ATTACHED TO THE DECIDUAL WALL. (T. H. Bryce.)

The villi are now occupied by a core of vascular mesoderm. They are covered by a syncytium (continued over the decidua), within which is a layer of epithelium cells. *f.v.*, fœtal vessels; *m.v.*, maternal vessels; *m*, mesoderm of chorion; *a*, a villus cut across; *b*, attachment of a villus; *sy*, syncytial covering to villi continued at *sy'* on to decidua; *ep*, epithelial layer under syncytium.

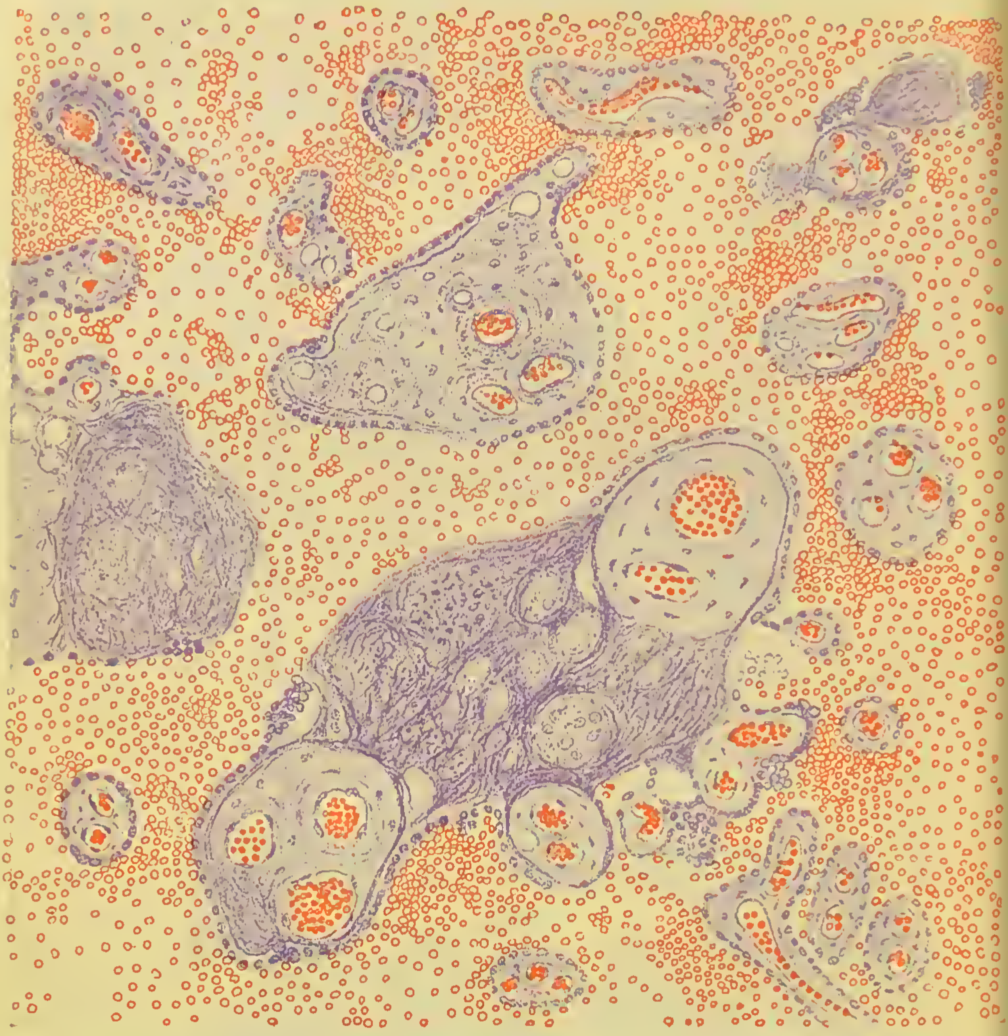

FIG. 512.—SECTION OF A PLACENTA AT FULL TIME. (T. H. Bryce.) From a preparation by J. H. Teacher.

One or two of the villi show fibrinous degeneration. For the sake of distinction the fœtal blood-corpuscles are represented as solid dots, the maternal as circles.

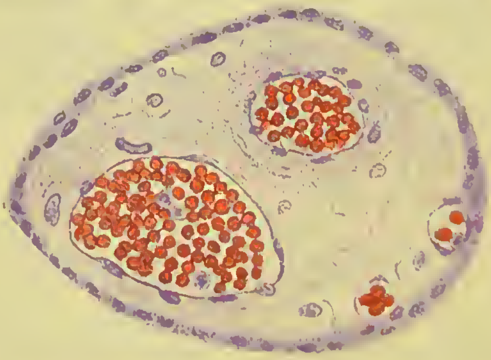

FIG. 513.—SECTION OF A VILLUS FROM A PLACENTA AT THE SEVENTH MONTH. (T. H. Bryce.)

to fibrous septa which extend from this wall to the chorion, and partly subdivide the placenta into loculi.

A section across the placenta at full time shows it to be bounded on the fœtal side by the chorion, covered by the smooth amnion, and on the maternal side by the thin and somewhat uneven detached part of the decidua—a separation having occurred in the substance of the decidua when the placenta becomes detached from the uterus. Between these two boundaries is a spongy mass which in sections examined under the microscope (fig. 512) appears to be formed of a more or less continuous blood space in which an enormous number of fœtal villi are cut in various directions.

Each villus (fig. 513) is formed of a jelly-like connective tissue covered by a layer of epithelial cells, which appear to be united with one another to form a syncytium. Within the larger villi arterioles and venules are seen (in some capillaries also), within the smaller only capillaries. Some of the villi at times appear to be undergoing fibrinous degeneration (fig. 512, F).

LESSONS XXXIX. AND XL.

STRUCTURE OF THE SPINAL CORD.

1. Sections of the spinal cord from the cervical, dorsal, and lumbar regions. If the human spinal cord cannot be obtained sufficiently fresh, that of a dog, cat, or monkey may be used. It is to be hardened by suspending it immediately after removal from the body in a tall jar of formol (10 per cent. solution). After a few days it may be transferred to alcohol. Sections are to be made either by the paraffin or celloidin method: the former is preferable for small cords. The sections may be stained by Nissl's method, which brings to view the nerve-cells and also stains the axis-cylinders of the nerve-fibres. If it is desired to stain by the Weigert-Pal method, which colours the medullary sheaths of the nerve-fibres, the pieces of cord should be placed in 2 per cent. bichromate of potassium solution or Müller's fluid (either at once or after formol) and should be left for about a month, after which they are cut by a freezing microtome. (For the details of these methods see Appendix.) Carminate of ammonia or thionin may also be employed to stain the nerve-cells and axis-cylinders.

Notice the relative extent of the grey as compared with the white matter in the different regions of the cord.

Sketch a section from each region under a low power. Sketch also a small portion of the white substance, two or three nerve-cells, and the central canal with its lining epithelium and surrounding neuroglia under the high power.

Measure the diameter of some of the nerve-fibres in the anterior columns, in the lateral columns, and in the posterior columns.

2. Tracts in the spinal cord. The conducting tracts of the spinal cord may be studied in two ways, viz.: (1) by preparing sections of embryonic cords (from the 5th to the 9th month), the sections being stained by the Weigert-Pal process (Flechsig's method); (2) by preparing sections from the cord of an animal in which either a complete section or a hemi-section has been performed about 15 days before the animal is killed, and staining thin pieces of the cord from below and from above the section by placing them in a solution consisting of two parts of Müller's fluid and 1 part of 1 per cent. osmic acid (Marchi's method, see Appendix). The cord must first be partly hardened by placing it for a few days in Müller's fluid.

Also Sherrin[illegible] [illegible]

The **spinal cord** is composed of grey matter in the centre and of white matter externally. It is closely invested by a layer of connective tissue containing numerous blood-vessels (*pia mater*), and less closely by two other membranes (fig. 514). One of these is an areolar membrane, resembling a serous membrane in general structure, but non-vascular and more delicate in texture (*arachnoid*). The other, which lines the vertebral canal, is a strong fibrous membrane known as the *dura mater*. At the middle of the anterior and posterior (ventral and dorsal) surfaces the pia mater dips into the substance of the cord in the *anterior* and *posterior median fissures*, so as to divide it almost completely into two lateral halves. These are, however, united by an isthmus or bridge, which is composed anteriorly of transversely crossing white fibres (*white or anterior commissure*), posteriorly of grey matter (*grey commissure*), in the middle of which is a minute canal lined by ciliated epithelium (*central canal*).

Each lateral half of the spinal cord contains a crescent of grey matter, which is joined to the corresponding crescent of the opposite side by the grey commissure. Of the two horns of the crescent the posterior or dorsal is the narrower and comes near the surface of the cord: close to it the bundles of the posterior nerve-roots enter the cord. The bundles of the anterior nerve-roots emerge from the anterior horn.

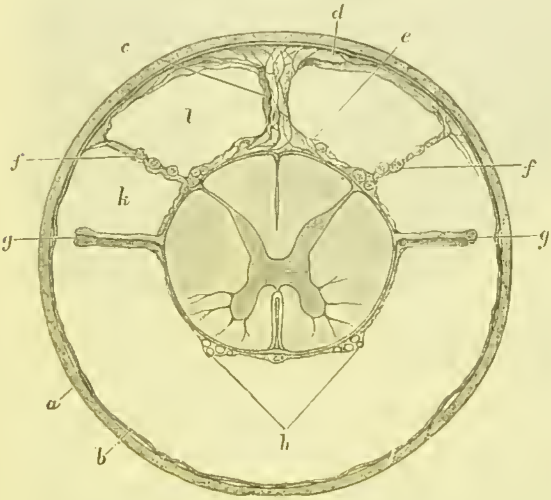

Fig. 514.—Section of the spinal cord within its membranes. (Key and Retzius.)

a, dura mater; *b*, arachnoid; *c*, septum of arachnoid; *d*, *e*, trabeculæ of arachnoid; *g*, ligamentum denticulatum; *f*, bundles of posterior root; *h*, bundles of anterior root; *k*, *l*, subarachnoid space.

According to Ingbert about 1,300,000 nerve-fibres enter the cord by the posterior roots, and about one-third that number leave it by the anterior roots.

The posterior root-fibres are derived from the cells of the spinal ganglia, which lie outside the cord; the anterior root-fibres from cells within the grey matter, chiefly from cells in the anterior horn, but also from some cells in the middle and posterior parts of the grey matter and (especially in the thoracic region) from cells in the intermedio-lateral tract (lateral horn). The latter probably furnish the autonomic (sympathetic) fibres of the anterior roots, while the cells of the anterior horn furnish the fibres which are distributed to the voluntary muscles.

The *white matter* of each half of the cord is subdivided by the approach of the posterior horn to the surface into two unequal columns—*antero-lateral* and *posterior*. A distinction is sometimes drawn between anterior and lateral portions of the antero-lateral

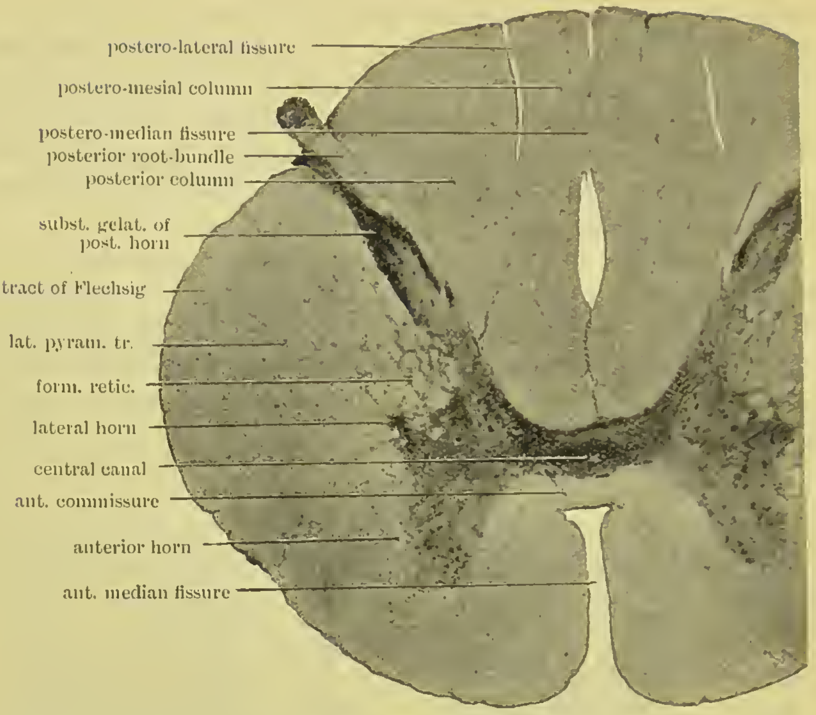

FIG. 515.—SECTION OF HUMAN SPINAL CORD FROM UPPER CERVICAL REGION. (Photograph.) Magnified about 8 diameters.

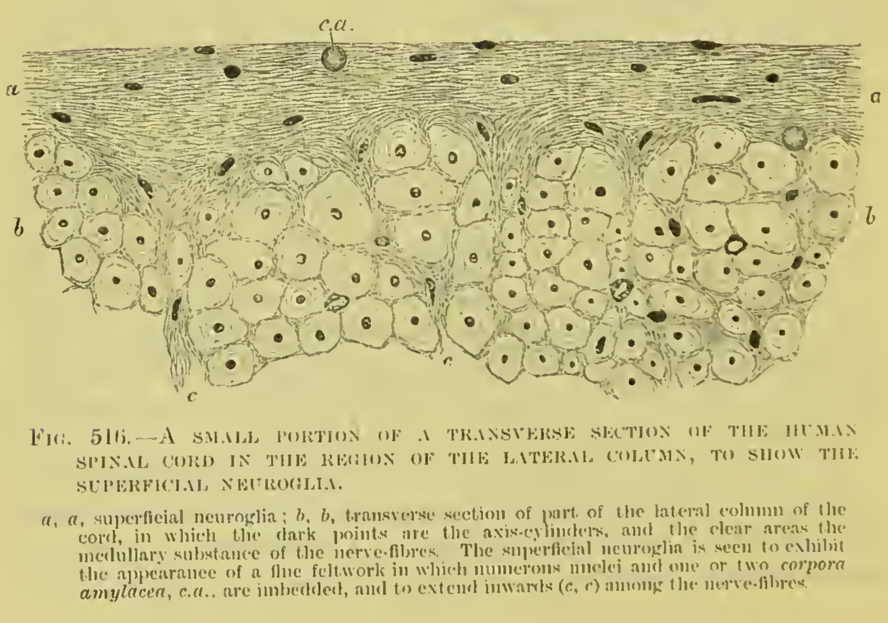

FIG. 516.—A SMALL PORTION OF A TRANSVERSE SECTION OF THE HUMAN SPINAL CORD IN THE REGION OF THE LATERAL COLUMN, TO SHOW THE SUPERFICIAL NEUROGLIA.

a, *a*, superficial neuroglia; *b*, *b*, transverse section of part of the lateral column of the cord, in which the dark points are the axis-cylinders, and the clear areas the medullary substance of the nerve-fibres. The superficial neuroglia is seen to exhibit the appearance of a fine feltwork in which numerous nuclei and one or two *corpora amylacea*, *c.a.*, are imbedded, and to extend inwards (*c*, *c*) among the nerve-fibres.

column, although there is no line of demarcation between them. In the upper part of the cord the posterior column is subdivided by a septum of connective tissue into two—the *postero-mesial column* or *funiculus gracilis*, and the *postero-lateral column* or *funiculus cuneatus*.

The white matter is composed of longitudinally coursing medullated nerve-fibres, which in sections stained with carmine or thionin appear as clear circular areas with a stained dot, the axis-cylinder, near the middle (fig. 516); while in sections stained by the Weigert-Pal method they appear as black circles with a clear centre. The nerve-fibres vary in size in different parts; on the whole those which are nearest to the surface of the cord are larger than those nearest to the grey matter, but there is a bundle of very small fibres (at M, fig. 517) opposite the tip of the posterior horn.

The medullated fibres are supported by *neuroglia*, which is composed of fibres and neuroglia-cells (figs. 228, 229). The neuroglia is accumulated in greater amount at the surface of the cord, underneath the pia mater (particularly, in the human cord, near the entrance of the posterior roots (fig. 516)), and it extends into the grey matter, in which it is especially abundant in the *substantia gelatinosa* at the apex (*caput*) of the posterior horn and around the central canal.

The *grey matter*, besides neuroglia, contains an interlacement of nerve-fibres and the arborisations of the dendrons of the nerve-cells which are imbedded in it.

Characters of the spinal cord in the several regions (figs. 517, 522). —In the *cervical region* the white matter, especially that of the lateral columns, occurs in largest proportion. The grey matter in the cervical enlargement is also in considerable amount, and it encroaches, especially in the upper part of the region, in the form of a network (*formatio reticularis*) upon the adjacent part of the lateral white column (fig. 515). The anterior horns are thick and the posterior slender. The postero-mesial column is distinctly marked off.

In the *dorsal region* the grey matter is small in amount, and both horns are slender. The whole cord is smaller in diameter than either in the cervical or lumbar region. The columns of nerve-cells known as Clarke's column and the intermedio-lateral column are well marked.

In the *lumbar region* the crescents of grey matter are very thick, and the white substance, especially the lateral columns, relatively small in amount. The isthmus lies nearly in the centre of the cord, whereas in the cervical and dorsal regions it is nearer the anterior surface.

In the part of the spinal cord from which the *sacral* and *coccygeal* nerve-roots take origin grey matter largely preponderates, the

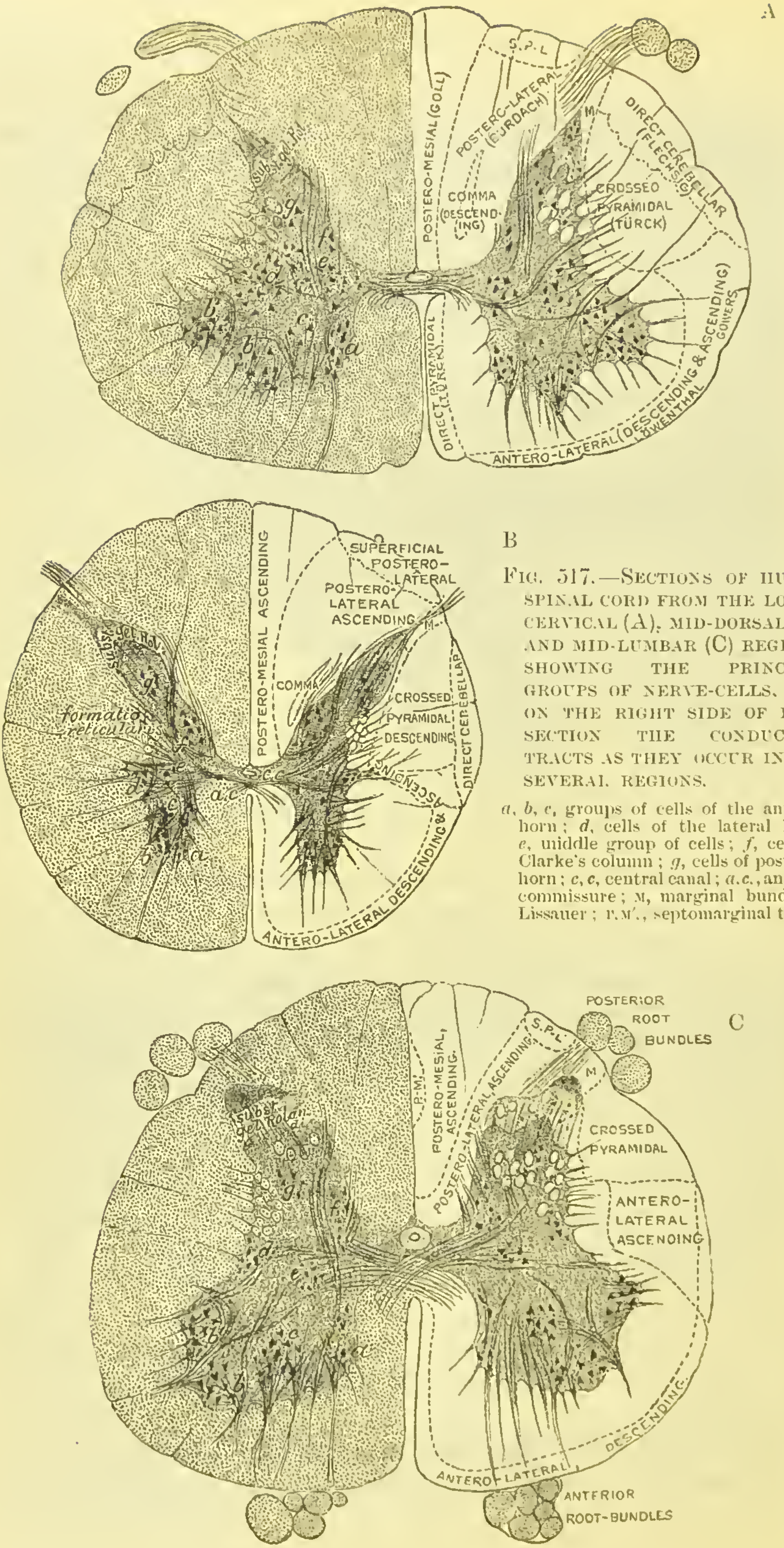

FIG. 517.—SECTIONS OF HUMAN SPINAL CORD FROM THE LOWER CERVICAL (A), MID-DORSAL (B), AND MID-LUMBAR (C) REGIONS, SHOWING THE PRINCIPAL GROUPS OF NERVE-CELLS, AND ON THE RIGHT SIDE OF EACH SECTION THE CONDUCTING TRACTS AS THEY OCCUR IN THE SEVERAL REGIONS.

a, *b*, *c*, groups of cells of the anterior horn; *d*, cells of the lateral horn; *e*, middle group of cells; *f*, cells of Clarke's column; *g*, cells of posterior horn; *c*, *c*, central canal; *a.c.*, anterior commissure; M, marginal bundle of Lissauer; P.M'., septomarginal tract.

crescents form thick irregular masses, and the grey isthmus is also of considerable thickness

TRACTS OF NERVE-FIBRES IN THE WHITE COLUMNS.

The course of the nerve-tracts in the spinal cord, and in other parts of the central nervous system, can be made out by the method of Flechsig, which involves the study of sections of the developing cord; for it is found that the formation of medullary substance occurs sooner in some tracts than in others, so that it is easy to make out the distinction between them. Thus, the peripheral nerves and nerve-roots become myelinated in the first half of the fifth month of fœtal life. Of the tracts of the spinal cord, those of Burdach and Goll (see below) are the first to be myelinated, then the tracts of Flechsig and Gowers, all of these being sensory or centripetally conducting, while the pyramid-tracts, which are motor or centrifugally conducting, do not receive their myelin sheath until after birth.[1]

Another method (that of A. Waller) consists of investigating the course which is pursued by degeneration of the nerve-fibres in consequence of lesions produced accidentally or purposely. Those tracts in which degeneration of fibres occurs below the lesion are termed "descending" tracts; those in which it occurs above the lesion are termed "ascending." This method, when combined with the staining process devised by Marchi, is by far the more valuable, since it enables even single fibres to be traced out.

The cells whence the fibres of any tract arise can be identified after a lesion of the tract by the chromatolysis or degeneration of Nissl which nerve-cells undergo after section of their axons (see pp. 177, 178).

Tracts of the posterior column.—1. *Tract of Goll.*—The fibres of the *postero-mesial column* belong to a tract which is known as the *tract of Goll* (fig. 518, 6). This consists of fibres derived from the posterior nerve-roots of the sacral, lumbar, and lower dorsal nerves, which, after having entered the postero-lateral columns, pass, as they ascend, towards the posterior median fissure and form a distinct tract, which is marked off from the rest of the posterior column in the cervical region by a slight furrow and a septum of pia mater (fig. 515). This tract ends amongst the cells of the *nucleus gracilis* of the medulla oblongata.

2. *Tract of Burdach.*—The *postero-lateral column* (*tract of Burdach*) is also composed of fibres of the posterior nerve-roots, which all run for

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[1] Flechsig finds that the fibres of the posterior roots are myelinated in at least three stages, and that the postero-lateral tract shows a corresponding differentiation into three chief parts: the *ventral*, *middle*, and *dorsal root-zones*. He suggests that this differentiation corresponds with functional differences of the fibres.

a certain distance in it before entering the grey matter of the cord or of the medulla oblongata. As each mass of posterior root-bundles enters the column close to the apex of the posterior horn it, so to speak, pushes the root-fibres which have already entered nearer to the median fissure; hence those which are derived from the lowest nerve-roots are nearest that fissure (in the tract of Goll), while those which are derived from the highest remain near the posterior horn (in the tract of Burdach). Many of the fibres of both tracts pass into the grey matter either immediately on entering the cord or in their course upwards; the rest are continued into the medulla oblongata, and those of the tract of Burdach end by arborising amongst the cells of the *nucleus cuneatus*.

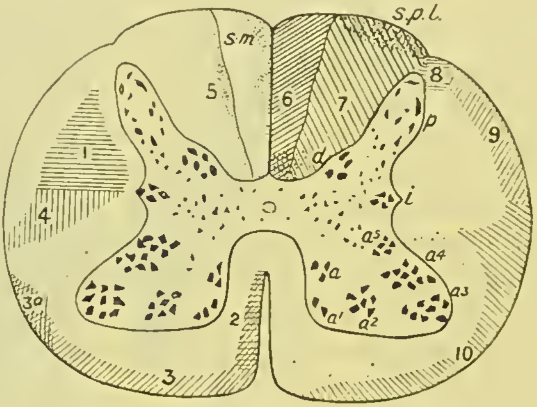

Fig. 518.—Diagram showing the ascending (right side) and descending (left side) tracts in the spinal cord.

1, Crossed pyramid-tract; 2, direct pyramid-tract; 3, antero-lateral descending; *3a*, bundle of Helweg; 4, prepyramidal; 5, comma; 6, postero-mesial; 7, postero-lateral; 8, tract of Lissauer; 9, dorsal cerebellar; 10, antero-lateral ascending or ventral cerebellar; *s-m*, septo-marginal; *s.p.l.*, superficial postero-lateral fibres (dorsal root zone of Flechsig); *a* to a^5, groups of cells in the anterior horn; *i*, intermedio-lateral group or cell-column in the lateral part of the grey matter; *p*, cells of posterior horn; *d*, dorsal nucleus of Stilling or cell-column of Clarke. The scattered dots indicate the situation of "endogenous" fibres (arising in grey matter of cord) having for the most part a short course.

3. *Comma tract.*—Besides the tracts of Burdach and Goll, which are wholly composed of long "ascending" fibres having their cells of origin in the ganglia on the posterior roots, there are a few fibres which have a shorter "descending" course in the posterior column. These are believed by some authorities to arise from descending branches of the posterior root-fibres, by others to arise from cells in the grey matter of the cord. They form the so called *comma tract* (fig. 518, 5).

Proprio-spinal or endogenous fibres of the posterior column.—These are a few fibres (*septo-marginal*), chiefly accumulated near the median fissure (*oval bundle*) and near the posterior surface (*median*

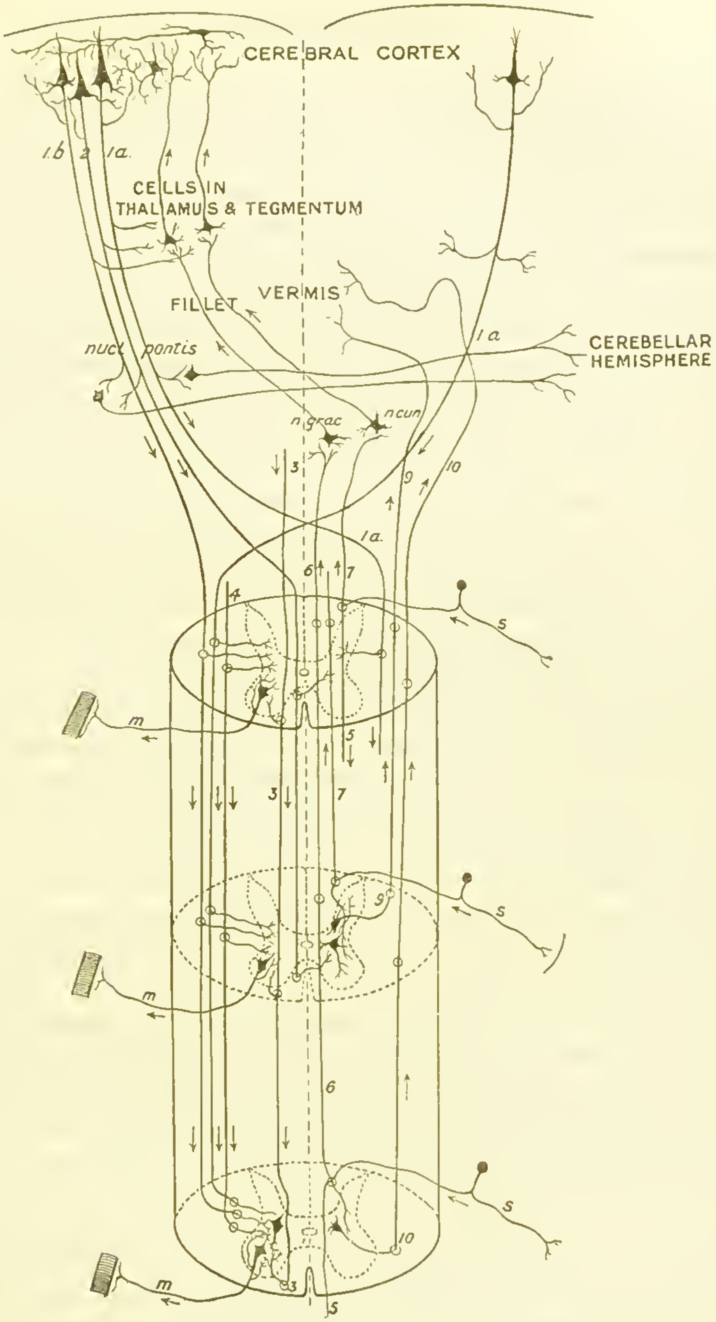

FIG. 519.—DIAGRAM SHOWING THE COURSE, ORIGIN, AND TERMINATION OF THE FIBRES OF THE PRINCIPAL TRACTS OF THE WHITE MATTER OF THE SPINAL CORD. (The numbers in this diagram refer to fibres of the tracts shown with corresponding numbers in fig. 518.)

“Descending” tracts:—*1a*, a fibre of the crossed pyramid-tract; *1b*, an uncrossed fibre of the pyramid-tract passing to the lateral column of the same side; *2*, a fibre of the direct pyramid-tract; *3*, a fibre of the antero-lateral descending tract; *4*, a fibre of the prepyramidal tract; *5*, fibres of the comma tract. “Ascending” tracts:—*6*, a fibre of the postero-mesial tract; *7*, fibres of the postero-lateral tract; *9*, one belonging to the dorsal cerebellar; *10*, a fibre of the ascending antero-lateral or ventral cerebellar tract. Also, *m*, motor nerves; *s*, sensory (afferent) nerves; *n.grac.*, nucleus gracilis; *n.cun.*, nucleus cuneatus; *nucl. pontis*, nucleus of pons. The arrows indicate the direction of the nerve-impulses.

triangle bundle), but also scattered in other parts of the column, which are derived from cells in the grey matter of the cord itself. All of the above take a "descending" course in the posterior column. Others which arise in the grey matter and have an "ascending" course are especially numerous in the ventral part of the column.

Descending tracts of the antero-lateral column.—1. *Pyramid-tract or cortico-spinal tract.*—At the posterior part of the lateral column there is a tract of moderately large "descending" fibres (intermingled with smaller fibres) which are found to run in the lateral column of the spinal cord from the opposite side of the brain, after having for the most part crossed at the decussation of the pyramids of the medulla oblongata (*crossed lateral-pyramid tract*, fig. 518, *1*; fig. 519, *1a*). Intermingled with the fibres of the crossed pyramid-tract in the lateral column are a few fibres of the pyramid which have not crossed in the medulla oblongata, and which are therefore derived from the cerebral cortex of the same side (*uncrossed lateral pyramid fibres*, fig. 519, *1b*). The large fibres which lie in the anterior columns next to the anterior median fissure, which are especially numerous in the upper part of the human cord, also belong to a portion of the same tract which has not undergone decussation (*direct pyramid-tract*, figs. 518, 519, *2*). The direct pyramid-tract is only found in man and the anthropoid apes; in some individuals it is absent, and it varies considerably in extent.

The pyramid-tracts are composed of "descending" fibres, which have their cells of origin in the cerebral cortex (precentral and paracentral gyri) and end by arborisations in the grey matter at the base of the posterior cornua of the spinal cord. In some mammals (rat, mouse, guinea-pig, sheep, kangaroo, squirrel, etc.) the pyramid-tracts are situated in the posterior columns of the cord, in others, including the monkey, dog, cat, and rabbit, they run wholly in the lateral columns. The pyramid-tracts are very small in the lower mammals, and are not found at all in vertebrates below mammals.

It has been calculated that there are about 80,000 fibres of the pyramid-tract in each half of the human cord. The pyramid-tracts are generally regarded as the paths along which volitional impulses are conveyed from the cerebral cortex to the spinal cord. But experiments have shown that they are not the only cortico-spinal paths nor even the most important in many animals, for the paralysis which results from their section is soon recovered from in most animals, whereas that resulting from section of the anterior column and adjacent part of the lateral column may be more marked and permanent. In man it appears to be the finer and more delicate movements which are permanently lost when the pyramid-tract is affected by disease.

2. *Tract of Loewenthal.*—Besides the pyramid-tracts there are four other "descending" tracts of fibres in the antero-lateral column. One of these (the *antero-lateral descending tract* or *tract of Loewenthal*, figs. 518, 519, *3*) lies on the side of the anterior median fissure, and extends along the margin of the cord in the "root" zone, even reaching the anterior part of the lateral column. These fibres are continued down, chiefly from the *posterior or dorsal longitudinal bundle* (*bulbo-spinal and ponto-spinal fibres*) of the medulla oblongata and pons, partly from other sources which will be afterwards referred to. They end by arborisations in the anterior horn. Similar arborisations pass from the posterior longitudinal bundle to the nuclei of the motor cranial nerves. This tract is mainly uncrossed.

3. *Rubro-spinal tract.*—Another "descending" tract in the antero-lateral column lies just in front of the crossed pyramid-tract; this is the *prepyramidal or rubro-spinal tract* (figs. 518, 519, *4*). Its fibres end by arborising in the grey matter of the middle of the crescent; the situation of its cells of origin is the red nucleus of the tegmentum in the mid-brain. This tract is also known as *Monakow's tract.* Some of its fibres are stated to be derived from cells in the reticular formation of the pons and medulla oblongata.

4. *Tecto-spinal fibres.*—Intermingled with the fibres of the rubro-spinal tract (but far fewer in number in man) are fibres derived from the quadrigeminal bodies of the opposite side. These fibres form a part of the *tecto-spinal tract.* Another part of this tract (*ventral longitudinal bundle*) passes into the anterior column of the cord in the tract of Loewenthal above mentioned.

5. *Olivo-spinal tract.*—Lastly, a small triangular group of "descending" fibres traceable from the neighbourhood of the olive in the medulla oblongata, and passing down the cervical cord in the anterior part of the lateral column (fig. 518, *3a*), (the exact origin and destination of the fibres is unknown) is termed the *bundle of Helweg* or *olivo-spinal tract.*

Ascending tracts of the antero-lateral column.—1. *Tract of Flechsig.*—This is a well-marked tract, which is however only distinct in the cervical and dorsal regions, where it lies external to the crossed pyramid-tract. It consists of large fibres which are derived from the cells of Clarke's column (fig. 518, *d*) and which pass up into the cerebellar vermis by way of the inferior peduncle of the same side (*dorsal spino-cerebellar bundle* or *direct cerebellar tract of Flechsig*, fig. 517; figs. 518, 519, *9*; 520, *b*, *b'*).

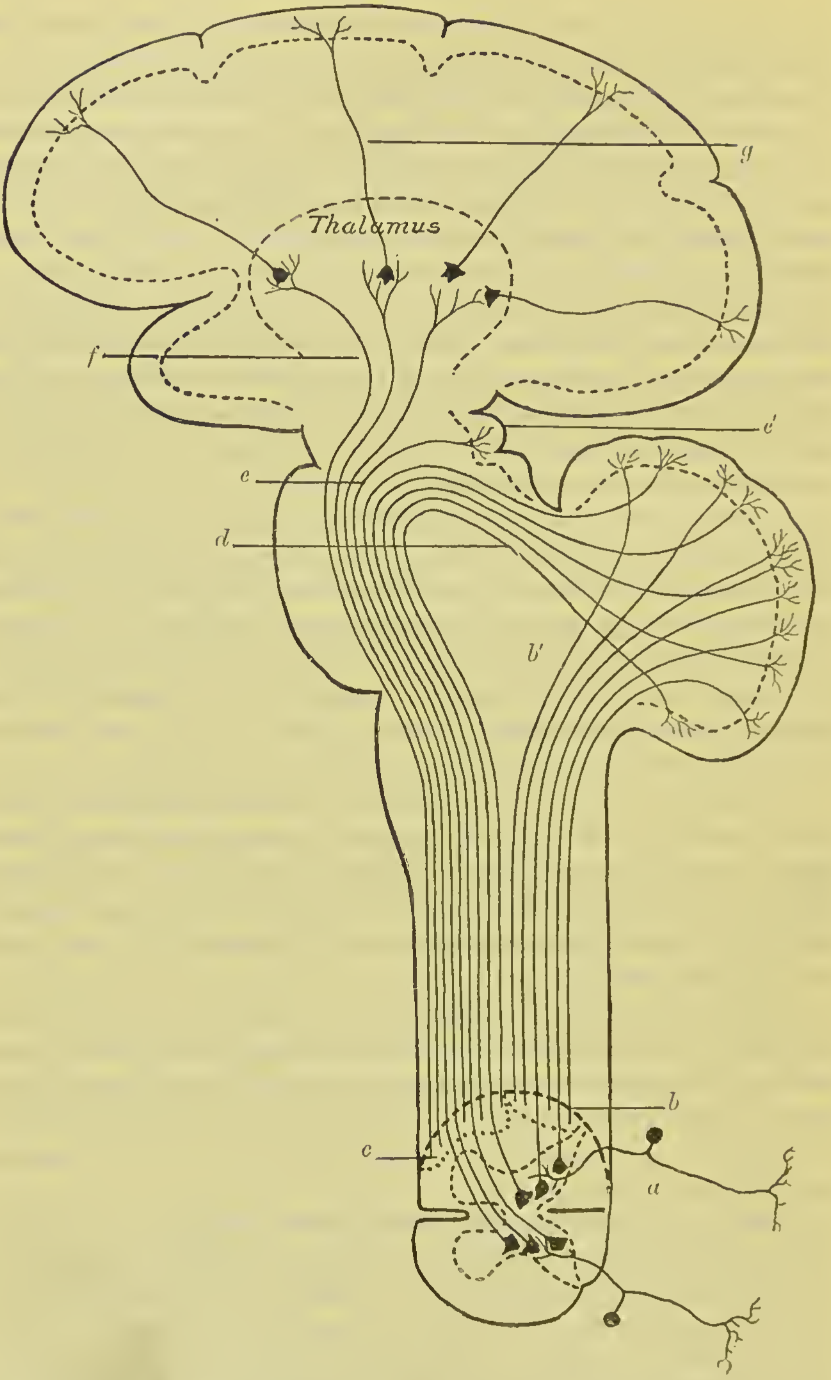

FIG. 520.—DIAGRAM SHOWING THE COURSE OF THE TRACTS OF FLECHSIG AND OF GOWERS IN THE SPINAL CORD AND THEIR CONTINUATIONS TO THE CEREBELLUM, CORPORA QUADRIGEMINA, THALAMUS AND CORTEX CEREBRI.

a, posterior root-fibres; *b*, tract of Flechsig, passing at *b′*, by the restiform body to the cerebellar vermis; *c*, tract of Gowers; *d*, passage of most of its fibres along the superior peduncle to the cerebellum; *e*, fibres to the corpora quadrigemina, *e′*; *f*, others to the thalamus; *g*, fibres from thalamus to cerebral cortex.

2. *Tract of Gowers.*—This is situated more anteriorly, lying in front of the crossed pyramid and direct cerebellar tracts in the lumbar region; while in the dorsal and cervical regions it forms a narrow band of fibres curving round close to the external surface of the cord, and extending even into the anterior column. It was termed the *antero-lateral ascending tract* by Gowers (figs. 518, 519, *10*). Its fibres are partly intermingled with those of the antero-lateral descending tract. Most of the fibres of the tract of Gowers are connected with the vermis of the cerebellum, constituting the *ventral spino-cerebellar bundle*, which passes to that organ over and parallel with the superior cerebellar peduncle (fig. 520). Both in the cord and medulla oblongata it gives off fibres to join the tract of Flechsig and to pass to the cerebellum by the inferior peduncle. According to Van Gehuchten, confirmed by Collier and Buzzard, the tract of Gowers gives off a few fibres to enter the opposite cerebellar hemisphere by the middle peduncle.

Some of the fibres of the antero-lateral ascending tract (*spino-tectal fibres*) are continued up to the corpora quadrigemina. Others pass into the tegmentum of the crus cerebri, where they can be traced as far as the lower part of the thalamus (*spino-thalamic fibres*).

The fibres of Gowers' tract appear to take origin from the cells of Clarke's column, especially from its lower part. This at least is the case with the cerebellar fibres. But the quadrigeminal and thalamic fibres are believed to arise from cells situated in the middle and posterior parts of the grey crescent, partly on the same but chiefly on the opposite side of the cord.

3. *Tract of Lissauer.*—Lastly, there is another small tract of fibres which undergoes degeneration above the point of section. This is the *marginal bundle of Lissauer* (marked M in fig. 517). It is formed by fine fibres from the posterior roots.

Other portions of the antero-lateral columns near the grey matter which are differentiated by the method of Flechsig are probably short tracts uniting adjacent portions of the grey matter of the cord.

Proprio-spinal or endogenous fibres of the antero-lateral column.—Sherrington has shown that in the dog the lateral column in the dorsal region of the cord contains a certain number of long fibres which take origin in the cervical, dorsal and upper lumbar segments and are traceable down to the lumbo-sacral enlargement. These must serve to convey excito-reflex impulses from the upper to the lower parts of the body. Probably similar fibres arise all along the cord from the cells of the lateral column and pass upwards as well as downwards.

A tract of endogenous fibres has been observed in man close to the anterior median fissure lying amongst the fibres of the direct pyramid-tract. This is known as the *anterior sulco-marginal tract* of Marie.

The antero-lateral column contains also many endogenous fibres, both ascending and descending, derived from cells in the grey matter of the cord, which have only a short course, serving to connect adjacent segments.

GREY MATTER OF CORD.

The nerve-cells which are scattered through the grey matter are in part disposed in definite groups. Thus there are several groups of large multipolar nerve-cells in the anterior horn in the cervical and lumbar enlargements (fig. 517), although in other regions of the cord the number of groups in this situation is reduced to two, a mesial and a lateral. The larger groups in the enlargements correspond with segments of the limb (Van Gehuchten); thus there appear to be groups associated with foot, leg, and thigh, and with hand, arm, and shoulder movements respectively. The groups from which the motor nerves to the shoulder and arm muscles arise appear in somewhat higher segments of the cervical cord than those belonging to the hand muscles. The same holds good, *mutatis mutandis*, for the lumbar cord in relation to the leg and foot. Further, the larger groups show subdivisions which may be related to particular movements, *i.e.* to particular groups of muscles. In the case of the diaphragm there is a special cell-group or cell-column in the anterior horn of the cervical cord from which the fibres of the phrenic nerve arise, so that in this case a cell-group is set apart for a special muscle.

The axis-cylinder processes of the anterior horn cells mostly pass out into the corresponding anterior nerve roots (fig. 519, *m*; fig. 523, *j*), but a few send their axons to the anterior column of the opposite side through the white commissure (fig. 523, *m*) or to the anterior or lateral column of the same side (*l*, *n*). It is noteworthy that in birds a few cells of the anterior horn send their axons into the posterior roots. A well-marked group of large rounded nerve-cells, best marked in the thoracic region, lies at the base of the posterior horn (*nucleus of Stilling, Clarke's column*, fig. 518, *d*; fig. 523, *u*). The cells of Clarke's column send their axis-cylinder processes into the dorsal cerebellar tract (Mott), and if this tract be cut experimentally, the large cells of Clarke's column on the same side below the section undergo Nissl degeneration and eventually atrophy, but the degeneration does not affect all these cells unless the tract of Gowers be

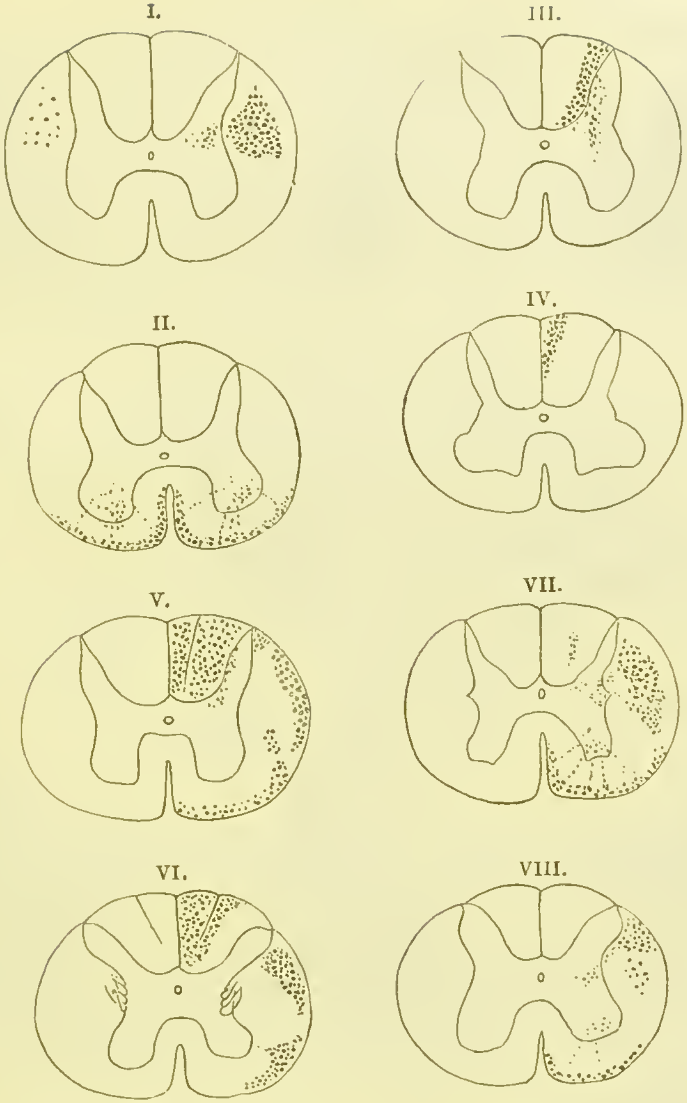

Fig. 521.—DIAGRAM OF SECTIONS OF THE SPINAL CORD OF THE MONKEY SHOWING THE POSITION OF DEGENERATED TRACTS OF NERVE-FIBRES AFTER SPECIFIC LESIONS OF THE CORD ITSELF, THE EFFERENT NERVE-ROOTS AND OF THE MOTOR REGION OF THE CEREBRAL CORTEX. (The degenerations are shown by the method of Marchi.) The left side of the cord is at the reader's left hand.

I. Degenerations resulting from extirpation of the motor area of the cortex of the left cerebral hemisphere.

II. Degenerations produced by section of the posterior longitudinal bundles in the upper part of the medulla oblongata.

III. and IV. Result of section of posterior roots of the first, second, and third lumbar nerves on the right side. Section III. is from the segment of cord between the last thoracic and first lumbar roots; section IV. from the same cord in the cervical region.

V. to VIII. Degenerations resulting from (right) semi-section of the cord in the upper thoracic region. V. is taken a short distance above the level of section; VI., higher up the cord (cervical region); VII., a little below the level of section; VIII., lumbar region.

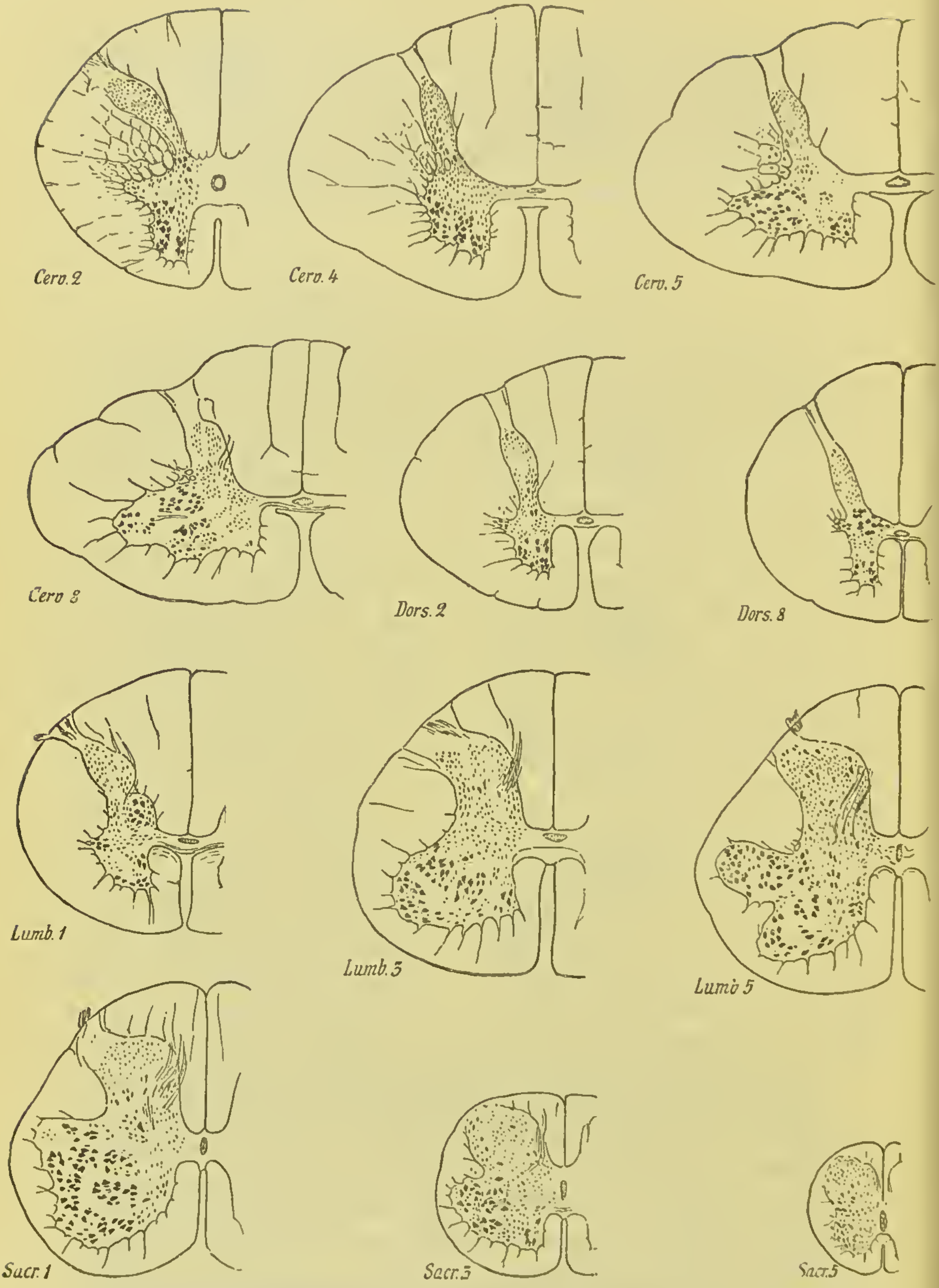

FIG. 522.—DIAGRAM OF SECTIONS OF HUMAN SPINAL CORD AT DIFFERENT LEVELS. (Edinger.)

The names refer to the origin of the corresponding nerve roots. The relative shape and size of the cord and grey matter, and the relative amounts of grey and white matter, and the principal cell-groups are shown.

also severed. There are a few small cells with short axons in Clarke's column which do not give rise to fibres of either of these tracts.

Another group is seen on the outer side of the grey matter lying in a projection which is sometimes known as the *lateral horn* (*lateral cell-column, intermedio-lateral column*, fig. 518, *i*). This is most distinct in the thoracic region as far up as the second thoracic segment. The axons from its cells for the most part leave the cord along with the anterior roots, and probably furnish the outgoing visceral and vascular fibres. Another group (*middle cell-column*) lies in the middle of the crescent (fig. 517, *e*). The cells of the posterior horn (*g*) are very numerous but are not collected into definite groups. Those of the substantia gelatinosa of Rolando send their nerve-fibre processes partly into the lateral, partly into the adjacent posterior columns (fig. 523, *s*, *t*).

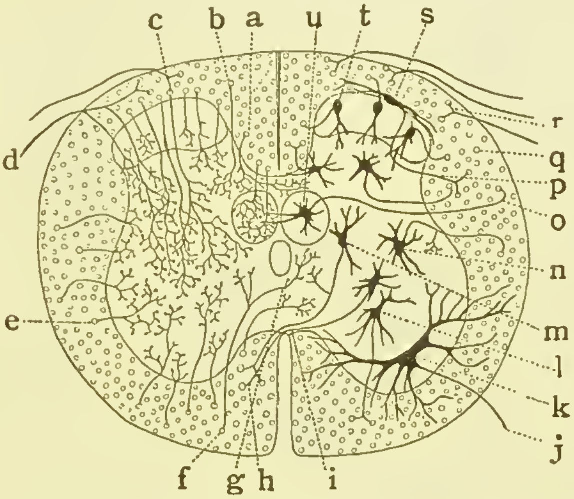

FIG. 523.—DIAGRAM SHOWING THE PROBABLE RELATIONS OF SOME OF THE CELLS OF THE CORD TO THE WHITE COLUMNS. On the left side the collaterals from the fibres of the white columns are shown passing into the grey matter. (Cajal.)

a, *b*, fibres of posterior column sending collaterals into the grey matter; *c*, *d*, fibres of posterior root entering posterior column; *e*, *f*, collaterals passing from lateral and anterior columns into grey matter; *g*, *h*, *i*, fibres of white commissure; *j*, anterior root-fibre springing from *k*, cell of anterior horn; *l*, *m*, *n*, other cells of grey crescent sending their axons into the white matter; *o*, axon of cell of Clarke's column passing into the dorsal cerebellar tract; *p*, axon of cell of substantia gelatinosa; *q*, fibre of dorsal cerebellar tract; *r*, fibre of posterior root passing to tract of Lissauer; *s*, *t*, cells of substantia gelatinosa; *u*, cell of Clarke's column.

The cells which send their axons into the adjacent parts of the white columns but not into any special tract are sometimes termed the "cells of the white columns."

The connection of nerve-roots with spinal cord.—The *anterior* or *ventral roots* leave the anterior horn in a number of bundles. Most of their fibres are directly continued from the nerve-cells in the anterior and lateral horns, and according to Golgi in part also from cells in the posterior horn. These cells, from which the anterior root-fibres arise, are surrounded by an interlacement of ramified nerve-endings, which are derived from various sources, especially the axons of cells of the posterior horn, from collaterals of the posterior root-fibres (see below), and from those of the fibres of the adjacent white columns.

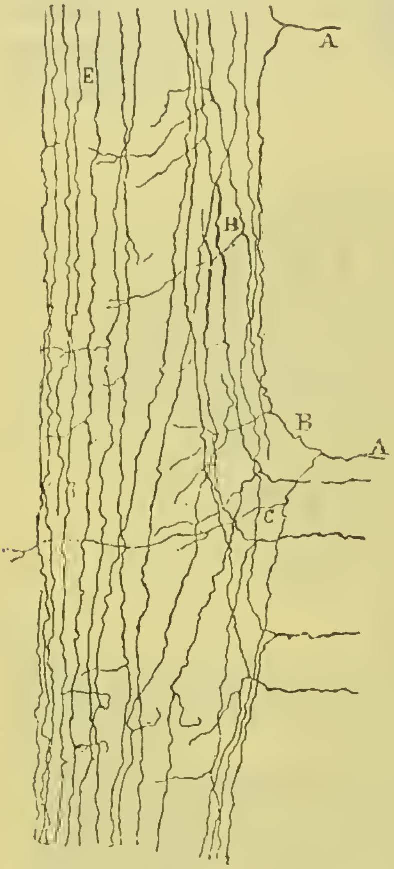

FIG. 524.—FROM A LONGITUDINAL SECTION OF SPINAL CORD, SHOWING THE ENTRANCE OF POSTERIOR ROOT-FIBRES. (Cajal.)

A, A, fibres entering the postero-lateral column, and bifurcating into an ascending and descending division; B, C, collaterals passing from them into the grey matter; E, other fibres of the posterior white columns also giving off collaterals.

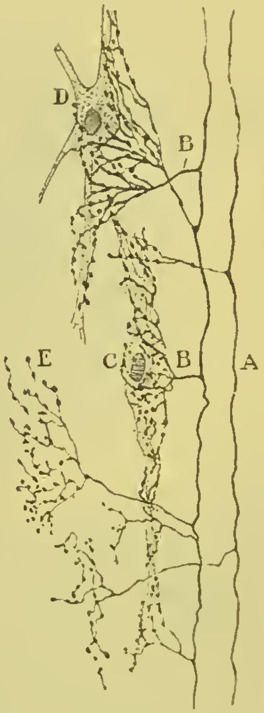

FIG. 525.—ARBORISATION OF COLLATERALS FROM THE POSTERIOR ROOT-FIBRES AROUND CELLS IN THE POSTERIOR HORN OF GREY MATTER. (Cajal.)

A, fibres of posterior column derived from posterior root; B, collaterals; C, D, nerve-cells in grey matter surrounded by the arborisations of the collaterals; E, an arborisation shown separately.

The fibres of the *posterior* or *dorsal roots* originate in the cells of the posterior root ganglia and pass into the postero-lateral column (see diagram, fig. 519), but the smallest fibres enter the marginal bundle of Lissauer, and some pass directly into the posterior horn of grey matter. On entering the spinal cord the fibres bifurcate (fig. 524), one branch passing upwards, the other downwards. Both from the main fibre and from its branches collateral fibres pass at frequent intervals into the grey matter, and end in arborisations of fibrils which envelop the nerve-cells both of the posterior (fig. 525) and of the anterior horn, and in the dorsal region the cells of Clarke's column and those of the intermedio-lateral column. Many of the main fibres also ultimately end in a similar manner in the grey matter, some after a short course only, but others after a long course. But a considerable number of fibres pass upwards in the postero-lateral and postero-mesial columns (in the latter especially those of the lower spinal nerves), until they arrive at the medulla oblongata, where they end in terminal arborisations around the cells of the nucleus gracilis and nucleus cuneatus.

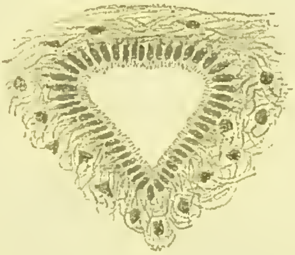

FIG. 526.—SECTION OF THE CENTRAL CANAL OF THE SPINAL CORD OF A CHILD, SHOWING ITS CILIATED EPITHELIUM AND THE SURROUNDING CENTRAL NEUROGLIA. Moderately magnified.

The **central canal** of the spinal cord is lined by columnar ciliated epithelium-cells (*ependyma*) which are surrounded by a quantity of neuroglia. The cells are best seen in the spinal cord of animals and in the child (figs. 526, 527); in the human adult they have frequently become proliferated, and cilia are no longer present. In the early embryo their fixed extremities extend through the whole thickness of the cord to reach the pia mater. This condition is permanent in the cord of many of the lower vertebrata.

Blood-vessels of the spinal cord.—The blood-supply of the grey matter is derived mainly from a series of arterioles, which come off from the mesially situated anterior spinal artery, pass into the anterior median fissure, and at the bottom of this divide each into two branches, one for the

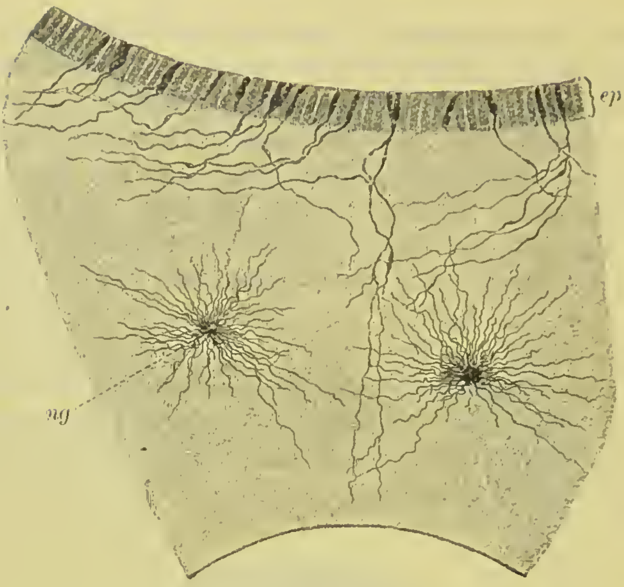

FIG. 527.—PART OF EPITHELIUM OF CENTRAL CANAL OF NEW-BORN CHILD, STAINED BY GOLGI'S METHOD. (Sobotta.) × 120.
ep, epithelium ; *ng*, neuroglia cells in adjacent grey matter.

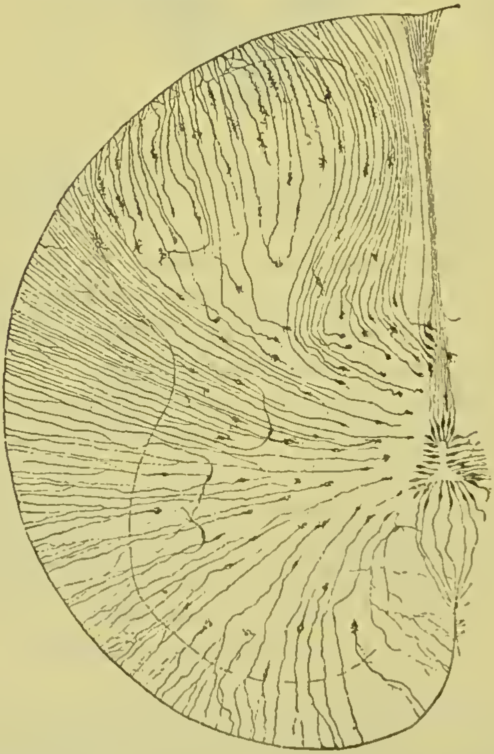

FIG. 528.—SECTION OF CORD OF EMBRYO, SHOWING SOME OF THE EPENDYMA CELLS DETACHED AND BECOMING CONVERTED INTO NEUROGLIA CELLS. (v. Lenhossék.)

grey matter of each lateral half of the cord. In the grey matter is a very close capillary plexus which is supplied not alone by the vessels just mentioned, but also by small arterioles, which converge from the small arteries of the pia mater, passing through the white matter, and supplying this as they pass through it. These arterioles are branches of the above-mentioned anterior spinal artery and of the posterior spinal arteries (which run on each side along the line of the posterior roots). The capillary plexus of the white matter is far less dense than that of the grey matter. It forms longitudinal meshes.

The veins of the spinal cord accompany the arteries. Two longitudinal venous vessels, accompanying corresponding anastomotic arterioles, are seen, one on either side of the central canal, in most transverse sections of the cord.

LESSON XLI.

THE MEDULLA OBLONGATA.

SECTIONS of the medulla oblongata (made in the same way as with the spinal cord): (*a*) at the level of the decussation of the pyramids, (*b*) just above the decussation, (*c*) opposite the middle of the olivary body, and (*d*) either through the uppermost part of the olivary body, or just above it.

The brain consists of three great morphological divisions associated with the three primary cerebral vesicles of the embryo; they are termed respectively the *hind-brain*, *mid-brain*, *fore-brain*.

The **hind-brain** forms the parts around the fourth ventricle, viz. the medulla oblongata or spinal bulb (myelencephalon), and above this the pons Varolii with the cerebellum (metencephalon); the **mid-brain** forms the region of the corpora quadrigemina (mesencephalon); the **fore-brain** the parts immediately above that region and centring around the third ventricle, including the optic thalami (thalamencephalon), as well as the corpora striata and cerebral hemispheres (telencephalon).

The structure of the **medulla oblongata** or **spinal bulb** can best be made out by the study of a series of sections taken from below upwards, and by tracing in these the changes which occur in the constituent parts of the spinal cord, taking note at the same time of any parts which may be superadded.

A section through the *region of the decussation of the pyramids* (fig. 529) has much the same form as a section through the upper part of the spinal cord, and most of the structures of the cord can be easily recognised. A considerable alteration of the grey matter is, however, produced by the passage of the large bundles of the crossed pyramid-tract from the lateral column of the spinal cord on each side through the root of the anterior horn and across the anterior median fissure to the opposite anterior column of the medulla oblongata, where, together with the fibres of the direct pyramid-tract, they constitute the prominent mass of white fibres which is seen on the front of the bulb, on each side of the middle line, and which is known as the *pyramid*. By this passage of fibres through the grey matter the tip of the anterior horn is cut off from the rest and becomes pushed as it were to the side; part of it appears as an isolated mass or masses of grey matter, one of which becomes known as the *lateral nucleus.* In sections just above the decussation of the pyramids a wavy band of grey matter makes its appearance on the lateral aspect of each pyramid, corresponding with a prominence on the surface which is known as the *olive.* The wavy or plicated grey matter is termed the *olivary nucleus* (figs. 530, 532).

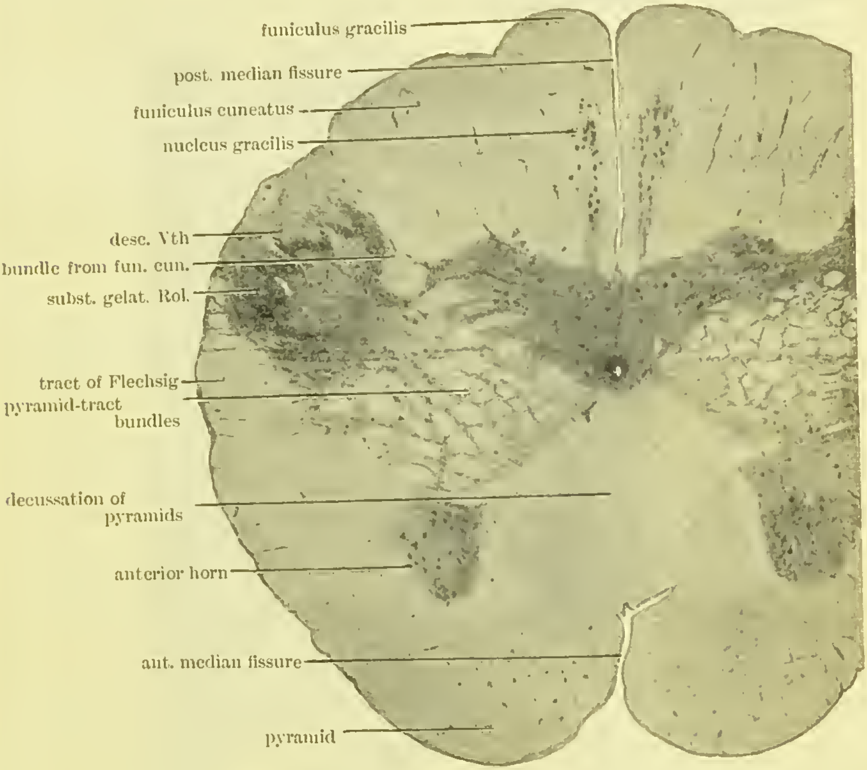

FIG. 529.—SECTION ACROSS THE LOWER PART OF THE MEDULLA OBLONGATA IN THE REGION OF THE DECUSSATION OF THE PYRAMIDS. Magnified 6½ diameters.

The **pyramids** (anterior pyramids) of the medulla oblongata are formed of fibres which originate in the motor region of the cerebral cortex, and which can be traced from the axons of large cells in the grey matter of that cortex through the white matter of the hemisphere, through the middle third or more of the internal capsule and crusta, through the pyramid bundles of the pons Varolii and into these structures (pyramids) of the bulb. As we have just seen, they pass at the lower limit of the bulb chiefly to the opposite or crossed lateral column of the cord, but partly to the lateral column of the same side, and, in man and anthropoid apes, partly to the anterior column. They collectively constitute the *tract of the pyramid*, which is smaller in the medulla oblongata than in the pons, since many of its fibres have left the main tract whilst within the pons and have passed across the middle line towards the grey matter on the dorsal aspect of the pons and medulla oblongata. Sometimes such a bundle of fibres, after passing towards the sensory nuclei in the lateral part of the medulla oblongata, does not end in them, but again comes ventralwards and joins the main or central part of the tract near its decussation (*bundle of Pick*).

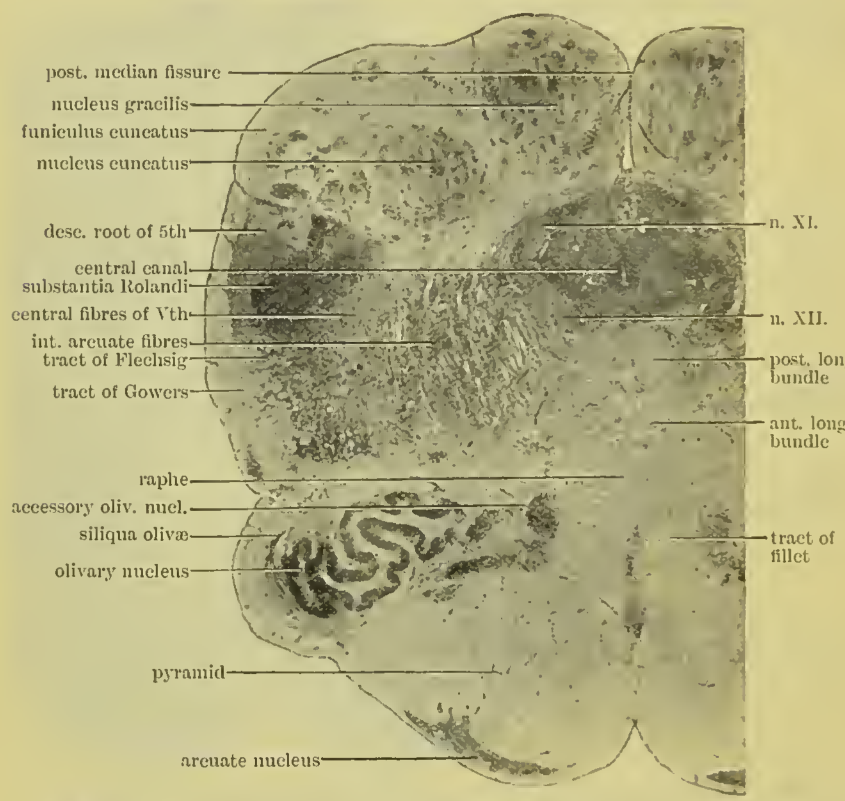

FIG. 530.—SECTION TAKEN IMMEDIATELY ABOVE THE DECUSSATION OF THE PYRAMIDS. Magnified 6½ diameters.

It is not a little remarkable that although the fibres of the pyramid-tract give off numerous collaterals to the grey matter of the cerebral cortex, the basal ganglia of the cerebrum, the substantia nigra of the mid-brain, the nuclei of the pons, and the base of the posterior horn of the spinal cord, no collaterals are seen to leave them in their course through the medulla oblongata, except a very few to the olivary nuclei. Various observers have described collaterals and terminations of the pyramid fibres as passing to the motor nuclei of the cranial nerves as well as to the anterior horns of the spinal cord, but statements to this effect must be received with caution, for although current in most text-books, they have not been substantiated by accurate observations. It is certain that most if not all of the fibres of the pyramid-tract end not in the ventral but in the dorsal part of the grey matter of the cord.

A change also occurs in the posterior horn in consequence of the increased development of the posterior column of white matter. This causes the posterior horns to be pushed towards the side, the V which they form with one another being thus opened out; at the same time the tip of the horn swells out and causes a prominence upon the surface of the medulla oblongata, which is known as the *tubercle of Rolando*. Its grey matter forms the prolongation of the sensory nucleus of the fifth nerve. On its outer side and partly embracing it is a bundle of fibres seen in every section of the medulla oblongata, and traceable up to the pons Varolii. This is the inferior or *descending root of the fifth nerve*—formerly known as the "ascending" root. Its fibres extend down as far as the upper cervical region of the spinal cord. Grey matter also soon becomes formed within the upward prolongations of the gracile funiculus (postero-mesial column), and of the cuneate funiculus (postero-lateral column), appearing at first as thin strands in the middle of the columns, but rapidly increasing in thickness so as eventually to occupy almost the whole of them, and forming the *nucleus gracilis* and the *nucleus cuneatus* respectively.

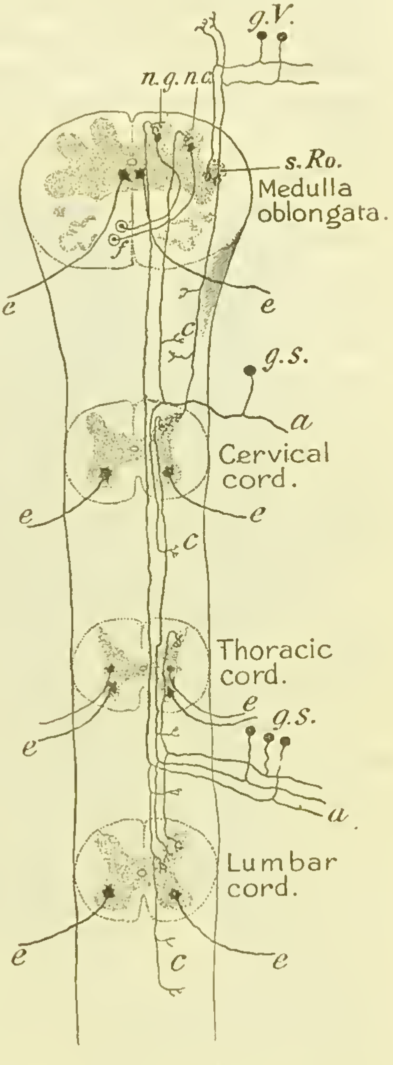

FIG. 531.—DIAGRAM, MODIFIED FROM CAJAL, TO SHOW THE COURSE OF THE POSTERIOR ROOT-FIBRES AFTER ENTERING THE CORD. (Schäfer.)

a, afferent fibres before entering ganglion; *g.s.*, spinal ganglion-cells; *g. V.*, ganglion of 5th nerve; *c*, descending branches (forming comma tract) giving off collaterals to grey matter. The ascending branches are shown partly ending in grey matter of posterior horn, partly in the nucleus gracilis (*n.g.*) and nucleus cuneatus (*n.c.*) of the medulla oblongata; *s.Ro.*, substantia Rolandi; *f*, fibres of fillet arising in nuclei of medulla oblongata; *e*, efferent nerve-fibres.

It is in these nuclei that the fibres of Goll's and Burdach's tracts, which are continued up from the posterior columns of the spinal cord, find their ultimate ending in complicated arborisations amongst the cells of the nuclei. These nuclei do not, however, receive all the ascending branches of the posterior root fibres, for a considerable number of these have already disappeared by entering the grey matter of the cord, in which they also end by arborisation amongst its cells. The cells of the nucleus gracilis and nucleus cuneatus are small or of moderate size with long dendrons. Their axons pass as internal arcuate fibres through the reticular formation into the inter-olivary layer, cross the median raphe dorsal to the pyramids (fig. 531), and then turn upwards, constituting the *tract of the fillet.* This tract, which in its lowest part is thus formed by the nerve-fibres which belong to the second relay (or second neurones) of one of the sensory spinal paths, is reinforced in the higher regions of the medulla oblongata and in the pons by fibres derived from cells of the sensory nuclei of the cranial nerves. The majority of its fibres end in the lateral nucleus of the thalamus, but some pass to both the anterior and posterior corpora quadrigemina.

According to Van Gehuchten the fibres of the fillet which are derived from the nucleus cuneatus lie dorsally to those which are derived from the nucleus gracilis.

The continuation of the *central canal* of the spinal cord is still seen in the lower medulla oblongata (figs. 529, 530), but it comes nearer to the posterior surface and eventually opens out at the point of the calamus scriptorius of the 4th ventricle (fig. 532). The grey matter which surrounds it contains two well-marked groups of nerve-cells; the anterior (ventral) of these is the lower part of the *nucleus of the hypoglossal* or twelfth nerve, the posterior (dorsal), with smaller cells, that of the *vago-accessory* or tenth and eleventh. But most of the grey matter of the crescent becomes broken up, by the passage of bundles of nerve-fibres through it, into a *reticular formation* the production of which is already foreshadowed in the upper part of the spinal cord. Instead of the comparatively narrow isthmus which joins the two halves of the spinal cord, a broad *raphe* now makes its appearance; this is formed of obliquely and antero-posteriorly coursing fibres, together with some grey matter containing nerve-cells.

In the section at *about the middle of the olive* (fig. 533), it will be seen that a marked change has been produced in the form of the medulla oblongata and the arrangement of its grey matter, by the opening out of the central canal into the fourth ventricle. This causes the grey matter which lower down surrounded the central canal to be now spread out at the floor of that ventricle, and the collections of nerve-cells from which the hypoglossal and vagus nerves respectively arise, now, therefore, lie in a corresponding situation near the ventricular floor. At this level the outer small-celled group which corresponds with the nucleus of the spinal accessory in the lower part of the bulb has become the *dorsal nucleus of the vagus or tenth nerve*, and yet higher up the *dorsal nucleus of the glosso-pharyngeal or ninth nerve.* The nerve-bundles of the roots of these nerves can be seen in some of the sections (fig. 533) coursing through the thickness of the bulb and emerging, those of the hypoglossal just outside the pyramids, those of the vagus at the side of the medulla oblongata.

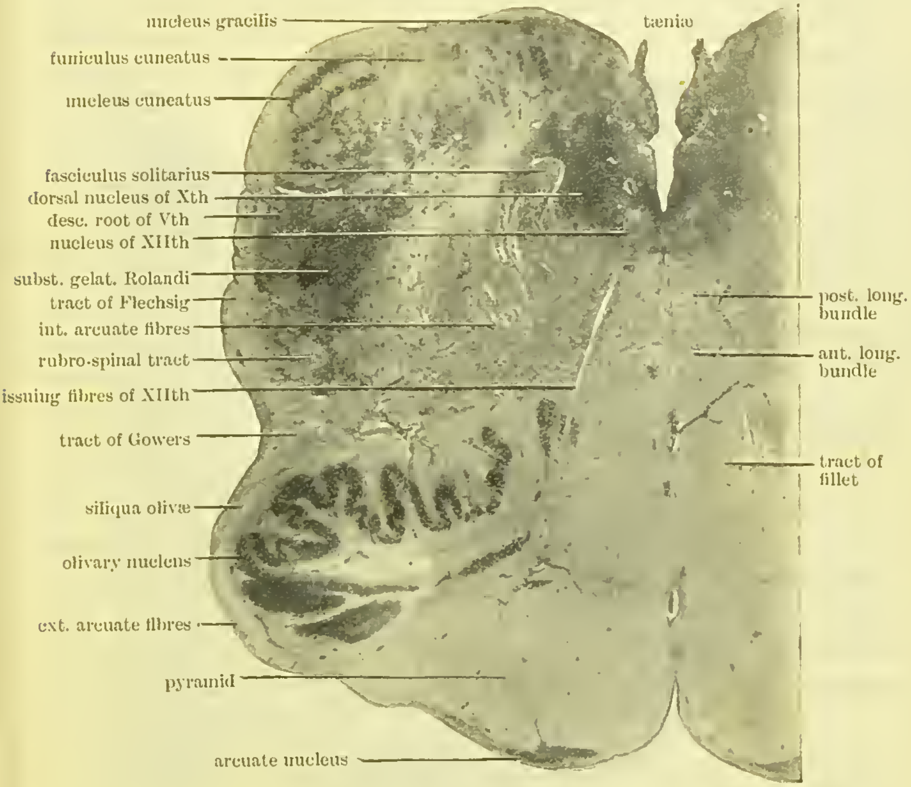

FIG. 532.—SECTION ACROSS THE MEDULLA OBLONGATA AT THE POINT OF THE CALAMUS SCRIPTORIUS OF THE 4TH VENTRICLE. Magnified 6½ diameters.

The posterior part of the section is chiefly occupied by the grey matter of the floor of the fourth ventricle, and by fibres which are passing obliquely upwards and outwards towards the cerebellum, forming its inferior crus (*restiform body*). The grey matter forming the nucleus of the funiculus gracilis and of the funiculus cuneatus has now almost disappeared, but in place of them and near the outer part of the floor of the fourth ventricle are seen some masses of grey matter with a number of bundles of nerve-fibres amongst them. The grey matter is the lower part of the principal nucleus of the vestibular nerve (see p. 443), and the white bundles are formed of descending branches of the fibres of that nerve. Below these structures is the descending root of the 5th, with its nucleus mesial to it.

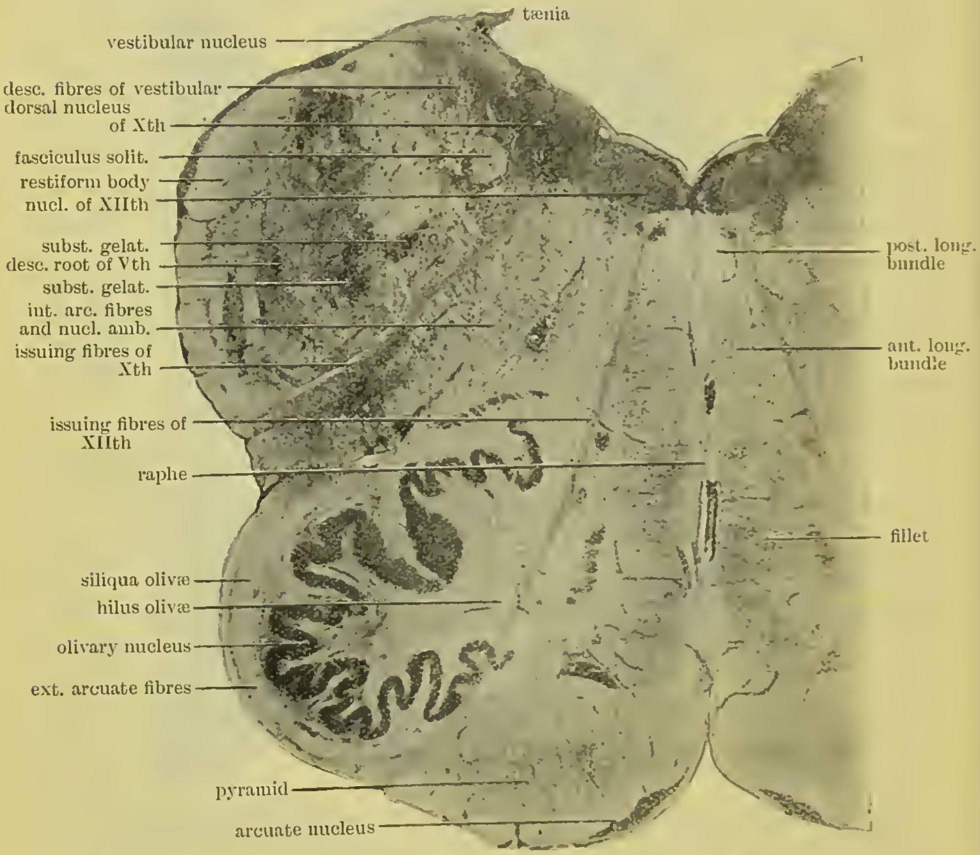

FIG. 533.—SECTION ACROSS THE MEDULLA OBLONGATA, AT ABOUT THE MIDDLE OF THE OLIVARY BODY. Magnified 6½ diameters.

The anterior part of the section is occupied in front by the pyramid, and behind this by a reticular formation (*reticularis alba*), composed of longitudinally coursing bundles of fibres belonging mainly to the *tract of the fillet* and to the *dorsal* and *ventral* (posterior and anterior) *longitudinal bundles*, interlaced with internal arcuate fibres that are passing across the raphe from the nuclei of the contralateral posterior columns into the fillet, and from the opposite olive into the restiform body.

The middle portion of the section consists for the most part of a similar reticular formation, but with more grey matter and nerve-cells (*reticularis grisea*). This is a development of the formatio reticularis of the cervical cord, and the longitudinally coursing white bundles in it are probably association fibres, derived from cells in the upper part of the cord. On the other hand the nerve-cells of this grey reticular formation in the medulla oblongata give origin to fibres which bifurcate and pass both upwards, probably serving as association fibres for the same area in the pons, and downwards towards the upper part of the cord. Some also are said to give origin to fibres, which either after traversing the raphe or passing directly to the same side as arched fibres, eventually enter the cerebellum through the inferior peduncle (Van Gehuchten).

Ventro-laterally is the *olive*, within which is developed a peculiar wavy lamina of grey matter containing a large number of nerve-cells; that is the *dentate nucleus of the olive.* The lamina is incomplete at its mesial aspect (*hilus olivæ*), and here a large number of fibres issue, and, passing through the raphe, course as internal arcuate fibres to the opposite restiform body, and thus to the cerebellum. Some, however, turn sharply round and course below the dentate nucleus, forming an investment and capsule to it (*siliqua olivæ*), and pass towards the restiform body of the same side: but the main connection of the olivary nucleus is with the cerebellar hemisphere of the opposite side. The olives receive numerous collaterals from the neighbouring white columns, including a few from the pyramids. Just dorsal, or dorso-lateral to the olive, is the continuation upwards of the *ventral spino-cerebellar bundle* (tract of Gowers) of the spinal cord; the continuation of the *dorsal spino-cerebellar bundle* (tract of Flechsig), just above it, is now passing into the restiform body.

A tract of fibres which arise within the thalamus passes over the lateral surface of the nucleus olivæ and ends within its grey matter (*thalamo-olivary tract, central tegmental tract* of Bechterew). The cells of the dentate nucleus have numerous dendrons; their axons all pass towards the hilus, where they emerge, and, for the most part, cross the raphe, pierce the opposite olivary nucleus, and pass, as already mentioned, into the restiform body (*olivo-cerebellar tract*).

Nerves arising from the medulla oblongata.—The 12th, 11th, 10th, 9th, and 8th nerves all take origin in the medulla oblongata, and their fibres may be seen emerging on either side, those of the 12th ventrally between the pyramid and olive, and those of the other three nerves in succession at the side of the medulla oblongata between the olive and restiform body.

The **XIIth** or **hypoglossal nerve** arises from a well-marked nucleus of large cells, similar to those of the anterior horn of the cord. This nucleus is situated:—in the lower part of the bulb, ventro-lateral to the central canal (fig. 530); in the upper part, near to the floor of the 4th ventricle, close to the middle line (figs. 532, 533). None of the fibres cross to the opposite side; according to Van Gehuchten, this is true of all the cranial nerves, except a few fibres of the 3rd nerve and the whole of the 4th nerve. The hypoglossal nucleus extends throughout about the lower two-thirds of the bulb (fig. 534, *nXII.*). It receives many collaterals from adjacent sensory tracts in the reticular formation and from the descending sensory nuclei of the 5th, 9th, and 10th nerves, as well as from the posterior longitudinal bundle. These form a plexus of fine fibrils within the nucleus which is highly characteristic. A similar plexus is seen in the oculo-motor nucleus.

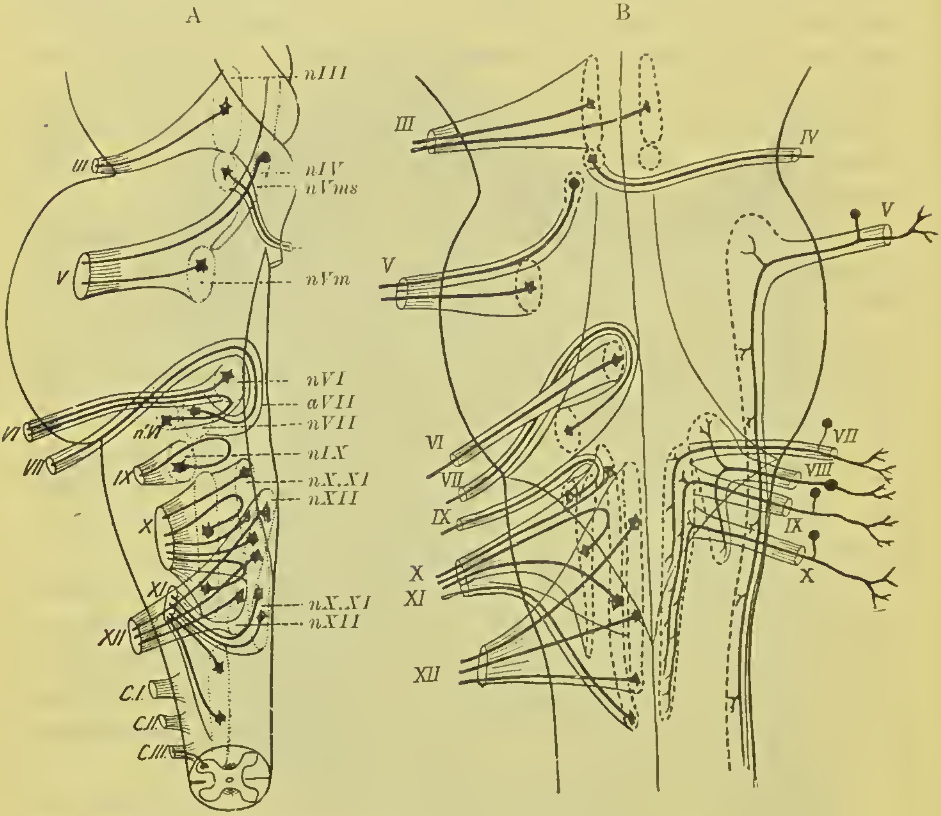

FIG. 534.—DIAGRAMS ILLUSTRATING THE ORIGIN AND RELATIONS OF THE ROOT-FIBRES OF THE CRANIAL NERVES.

A. Efferent fibres only: profile view.
B. Shows on the left the motor nuclei and efferent fibres (except those of the 4th nerve), and on the right side the afferent fibres: surface view.

Mesial to the hypoglossal nucleus, in the open part of the medulla oblongata, is the *nucleus of the fasciculus teres*, a column of moderate-sized cells which extends towards the lower margin of the pons and appears to receive fibres from the cerebellum (Edinger).

The **XIth nerve** or **spinal accessory** begins to take origin from cells in the lateral part of the grey matter of the spinal cord as low down as the 5th cervical nerve. Its fibres from the cord (spinal fibres) are those to the (voluntary) sternomastoid and trapezius muscles. They pass from the cells of origin in the lateral part of the anterior horn (*motor nucleus*) at first dorsalwards, and then take a sharp bend outwards through the lateral column to emerge at the side of the cord and medulla oblongata. The bulbar fibres (which join the vagus) take origin in a nucleus of relatively small cells which lies dorso-laterally to the central canal of the medulla oblongata and behind the hypoglossal nucleus. This nucleus is continuous above with the corresponding nucleus of the vagus, and with it forms the *dorsal accessory-vagus nucleus* (figs. 530, 532, 533, 534). Below, it extends nearly as far as the first cervical nerve; its upper part (vagal part) is in the floor of the 4th ventricle lateral to the hypoglossal nucleus, and extends nearly as far as the lower border of the pons. Of the whole nucleus about the lower two-thirds, *i.e.* as far as the lower end of the calamus scriptorius, gives origin to fibres of the accessory. These fibres, as already stated, join the vagus, to which they supply the motor fibres of the thyro-arytenoid muscles (Van Gehuchten). The 12th and 11th nerves are entirely efferent.

The **Xth nerve** or **vagus (pneumogastric)** contains both motor (efferent) and sensory (afferent) fibres. The efferent fibres arise (1) from the upper part of the dorsal accessory-vagus nucleus just described, (2) from a nucleus of grey matter containing large cells situated in the reticular formation (figs. 533, 535, *n.amb.*). This nucleus begins near the lower limit of the bulb and extends nearly to the facial nucleus, which it resembles in general position: it is known as the *nucleus ambiguus* (*ventral nucleus of the Xth nerve*). The axons of its cells are directed at first backwards and inwards and then turn sharply round in the lateral direction to join the rest of the issuing fibres of the nerve, coursing in the same manner as the spinal fibres of the accessory; indeed, this nucleus is continuous below with the column of cells from which those fibres take origin.

The sensory fibres take origin in the *ganglion of the root* and the *ganglion of the trunk* (*jugular* and *plexiform ganglia*) of the nerve, from unipolar cells like those of the spinal ganglia (fig. 535, *g*). They enter the medulla oblongata, and then bifurcate, one branch, a short (ascending) one, passing at once into the upper sensory or *principal nucleus*, the other, a long one, descending. The descending fibres (with similar fibres of the IXth and those of the *pars intermedia* of the VIIth) form the so-called *fasciculus solitarius* (figs. 532, 533, 535) (*descending root of facial, vagus, and glossopharyngeal*), which is traceable to the lower limit of the medulla oblongata; they end in grey matter which lies along its mesial border (*descending nucleus of facial, vagus, and glossopharyngeal*). This nucleus approaches the middle line as it descends, and in some animals terminates by joining its fellow of the opposite side over the central canal to form the *commissural nucleus* of Cajal. The upper sensory nucleus (*principal nucleus*), in which the short branches from the sensory root end, lies in grey matter near the floor of the ventricle, and is continuous with that which accompanies the fasciculus solitarius.

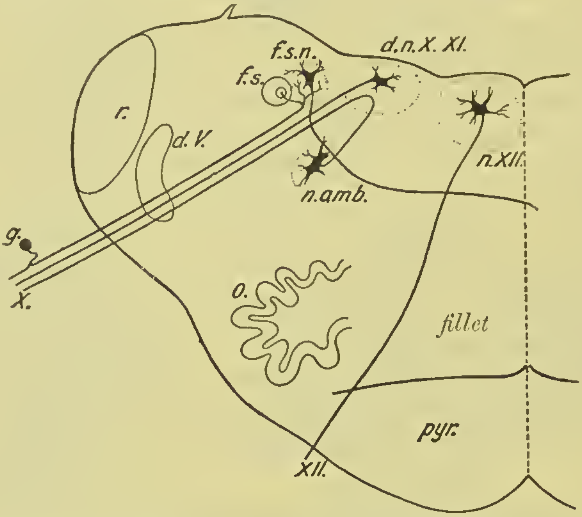

FIG. 535.—PLAN OF THE ORIGIN OF THE XIITH AND XTH NERVES.

pyr, pyramid; *n.XII.*, nucleus of hypoglossal; *XII.*, fibre of hypoglossal; *d.n.X. XI.*, dorsal nucleus of vagus and accessory; *n.amb.*, nucleus ambiguus; *f.s.*, fasciculus solitarius (descending root of vagus and glossopharyngeal); *f.s.n.*, its nucleus; *X.*, emerging motor fibres of vagus; *g*, cell in ganglion of vagus giving origin to a sensory fibre; *d.V.*, descending root of fifth; *r.*, corpus restiforme.

The **IXth** or **glossopharyngeal nerve** also contains both efferent and afferent fibres. The former have their cells of origin in a special nucleus which occupies a position similar to that of the nucleus ambiguus, but is mesial to the anterior end of that nucleus, and just below the nucleus of the facial (*motor nucleus of glossopharyngeal*). The afferent fibres of the nerve arise in the *upper* or *jugular* and *petrosal ganglia* from unipolar cells like those of the spinal ganglia. Their central axons enter the medulla oblongata, and, like other sensory fibres, bifurcate into two branches, ascending and descending. Their course is like those of the vagus, the descending passing down in the fasciculus solitarius (extending to about one-third of its length, Bruce),

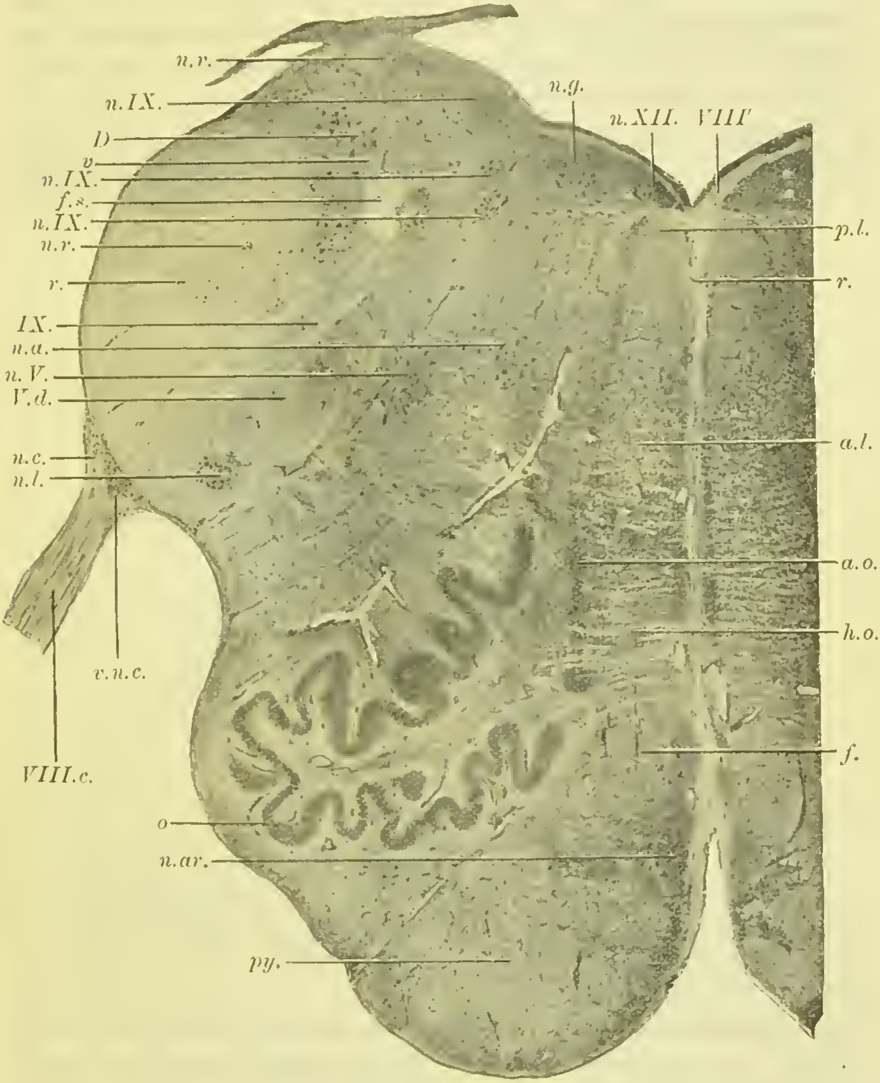

FIG. 536.—SECTION OF MEDULLA OBLONGATA AT THE LEVEL OF THE EIGHTH NERVE. Magnified about 6 diameters.

n.v., part of vestibular nucleus; *n.IX.*, parts of nucleus of ninth nerve; *D*, nucleus of Deiters; *v*, descending fibres of vestibular nerve; *f.s.*, fasciculus solitarius; *n.r.*, small nucleus in restiform; *r*, restiform body; *IX.*, fibres of ninth nerve; *n.a.*, nucleus ambiguus; *n.V.*, sensory nucleus of fifth nerve; *V.d.*, descending root of fifth; *n.c.*, part of dorsal cochlear nucleus; *VIII.c.*, cochlear division of eighth nerve; *v.n.c.*, ventral cochlear nucleus; *n.l.*, lateral nucleus; *o*, olivary nucleus; *n.ar.*, nucleus of arciform fibres; *py*, pyramid; *n.g.*, grey matter in floor of 4th ventricle; *n.XII.*, nucleus of twelfth; *VIII'*, fibres of cochlear nerve entering raphe; *p.l.*, posterior longitudinal bundle; *r*, raphe; *a.l.*, anterior longitudinal bundle; *a.o.*, accessory olivary nucleus; *h.o.*, fibres issuing from the hilus of the olive; *f*, fibres of fillet, and ending by arborising in the grey matter accompanying it (*descending root and nucleus*), while the ascending branches pass nearly horizontally backwards and inwards to a nucleus (*principal nucleus*) beneath the inferior fovea of the floor of the ventricle which is continuous with the upper end of the nucleus of the descending root. The arrangement is almost exactly a counterpart of that of the vagus shown in the diagram given in fig. 535.

According to Edinger the sensory nuclei of these nerves receive fibres from the cerebellum constituting a *cerebello-bulbar tract*, which is much better marked in lower vertebrates than in man and mammals.

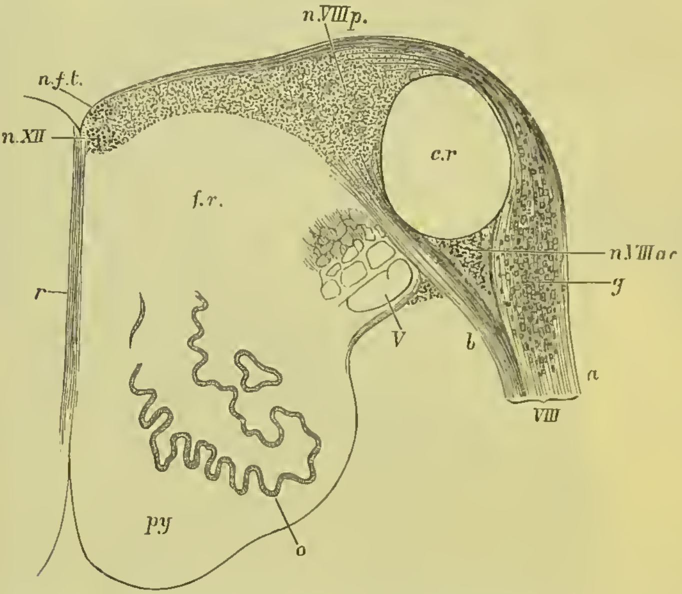

FIG. 537.—TRANSVERSE SECTION OF THE UPPER PART OF THE MEDULLA OBLONGATA. $\frac{4}{1}$. (Schwalbe.)

py, pyramid; *o*, olivary nucleus; *V*, descending root of the fifth nerve; *VIII.*, root of the auditory nerve, formed of two parts, *a*, cochlear, and *b*, vestibular, which inclose the restiform body, *c.r.*; *n.VIIIp.*, principal nucleus of the vestibular division; *n.VIIIac.*, ventral or accessory nucleus of the cochlear division; *g*, dorso-lateral nucleus of the cochlear division; *n.f.t.*, nucleus of the funiculus teres; *n.XII.*, nucleus of the hypoglossal; *r*, raphe; *f.r.*, reticular formation.

The **VIIIth nerve.**—A section taken *through the uppermost part of the olivary prominence* will still show very much the same form and structural arrangements as that just described (fig. 536). The *nucleus of the hypoglossal* (figs. 536, 537, *n.XII.*) is still visible in the grey matter of the floor of the ventricle near the middle line, but the nerve which is now seen connected with the lateral part is the *eighth* or *auditory* (*VIII.*), the bundles of which, as they enter the bulb, embrace the inferior crus of the cerebellum (*corpus restiforme*, *c.r.*), which is now passing into that organ. The origin of the *eighth nerve* is thus subdivided into two principal parts, known respectively as the *dorsal* or *cochlear* and the *ventral* or *vestibular* divisions (fig. 537).

The real origin of the nerve fibres in these roots is in the *ganglion of the cochlea* and the *ganglion of Scarpa* respectively. These ganglia, which are situated at the periphery within and near the internal ear, are composed of bipolar cells, of which the peripheral axons end by ramifying amongst the cells of the auditory epithelium, and the central axons form the cochlear and the vestibular divisions of the auditory nerve and pass into the medulla oblongata in the manner here described.

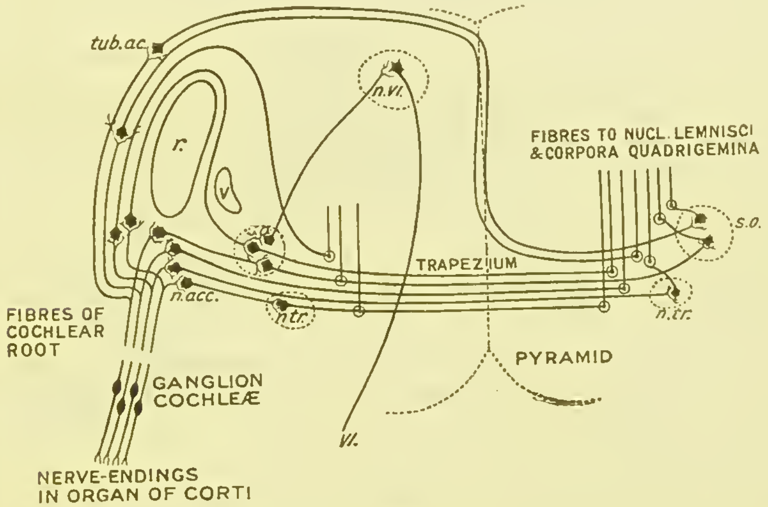

FIG. 538.—PLAN OF THE COURSE AND CONNECTIONS OF THE FIBRES FORMING THE COCHLEAR ROOT OF THE AUDITORY NERVE.

r, restiform body; *V.*, descending root of the fifth nerve; *tub.ac.*, tuberculum acusticum; *n.acc.*, accessory nucleus; *s.o.*, superior olive; *n.tr.*, nucleus of trapezium; *n.VI.*, nucleus of sixth nerve; *VI.*, issuing root fibre of sixth nerve.

The fibres of the **dorsal** or **cochlear division** (**cochlear nerve**) bifurcate as they enter the medulla oblongata. Each fibre divides into a thick and a thin branch. The thicker branches pass partly to a mass of ganglion cells which is wedged in between the two roots and the restiform body, and is known as the *ventral* or *accessory auditory nucleus* (figs. 537, 538, *n.acc.*), applying themselves with a peculiar form of terminal arborisation to the cells of this nucleus; partly over the restiform body to terminate in a prominent mass of grey matter which overlies that body, and also extends to the lateral part of the floor of the fourth ventricle at its widest part (*dorso-lateral nucleus, tuberculum acusticum*). The cells of the tubercle have a peculiar spindle shape and are set vertically to the surface. They appear to begin in the root itself, lying amongst the fibres of the nerve. Here they are sometimes spoken of as forming the "ganglion of the root." The thinner branches of the bifurcated cochlear fibres pass downwards for a certain distance and break up into a plexus of fine fibrils.

These two nuclei, viz., the accessory nucleus and the acoustic tubercle, are the nuclei of ending of the cochlear fibres. From their nerve-cells new fibres arise which continue the auditory path centrally (see fig. 538). Those from the accessory nucleus enter the *trapezium* —which consists of transverse fibres running behind the pyramid bundles of the pons Varolii—and pass in it partly to the superior olive and trapezoid nucleus of the same side of the pons, but mostly to the corresponding structures on the opposite side. Some end in those nuclei, but others merely traverse them, giving off numerous collaterals to them and to the *superior olives* and other nuclei close by (see p. 448), and then turn upwards in the lateral part of the tract of the fillet to pass ultimately towards the inferior corpora quadrigemina; in tending towards these structures at the side of the mid-brain they form the *lateral fillet*, or *fillet of Reil*, which is there conspicuous. Some of the fibres from the cells of the accessory nucleus do not pass directly to the trapezium, but first curve round the restiform body (Held); these form the most dorsally situated fibres of the trapezium. The fibres which arise in the acoustic tubercle pass for the most part over the floor of the fourth ventricle, where they are seen superficially as the *medullary* or *acoustic striæ*, and entering the raphe, traverse it from behind forwards, and then join the others from the accessory nucleus in their course to the superior olive and lateral fillet of which they constitute the deeper layer. A few fibres are directed into the fillet of the same side as their cells of origin.

Edinger states that, at least in the dog, all the fibres of the trapezium end in its nucleus or in the superior olivary nucleus, the central acoustic path being wholly continued, so far as the trapezium fibres are concerned, by fresh neurones, the cell-bodies of which lie in those nuclei, and the axons of which pass into the lateral fillet. On the other hand, from the cells in the tuberculum acusticum, the axons are said to be continued upwards in the opposite lateral fillet without the intervention of any corresponding nuclei. The lateral fillet passes above into the posterior colliculus of the mid-brain.

The accessory nucleus also receives fibres from the trapezium, which end by ramifying amongst its cells. These are perhaps derived from the accessory nucleus of the opposite side.

Both sets of fibres (from the accessory nucleus and tuberculum) give off collaterals near their origin, which terminate within these nuclei.

The **ventral or vestibular division (vestibular nerve)**, which enters a little in front of (above) the cochlear division, passes between the restiform body and the descending root of the fifth (fig. 537), to enter a mass of grey matter containing for the most part cells of small size, which is termed the *principal or dorsal nucleus* of the vestibular division. Here each of its fibres divides with a Y-shaped division into an ascending and a descending branch (fig. 539). The descending branches are collected into small bundles (*descending vestibular root*) which run downwards towards the lower part of the medulla oblongata, and gradually end by arborising around cells in the adjacent grey matter (*descending vestibular nucleus*), which is continued down from the principal nucleus. The ascending branches pass upwards on the inner side of the restiform body towards the nucleus tecti of the cerebellum. In their course they give off numerous collaterals which arborise round the large cells of two nuclei which occur in this part of the medulla oblongata and pons near the outer part of the floor of the fourth ventricle. These two nuclei are termed the *nucleus of Deiters* and the *nucleus of Bechterew* respectively (fig. 539).

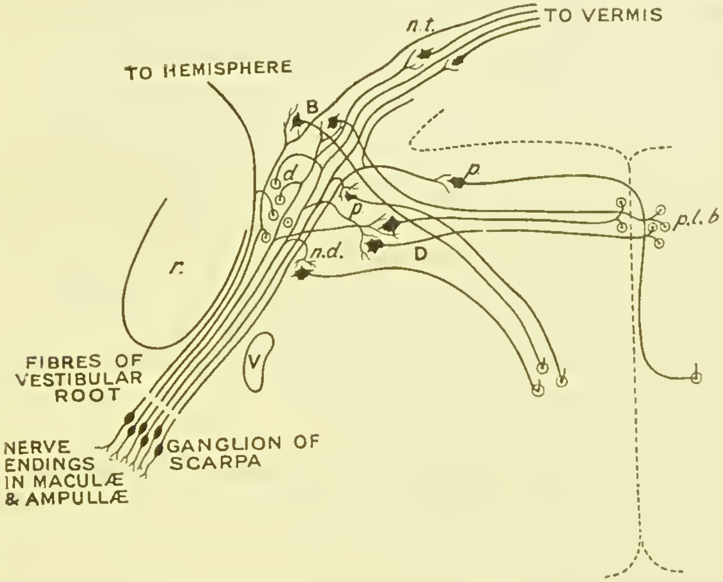

FIG. 539.—PLAN OF THE COURSE AND CONNECTIONS OF THE FIBRES FORMING THE VESTIBULAR ROOT OF THE AUDITORY NERVE.

r., restiform body; *V.*, descending root of fifth nerve; *p.*, cells of principal nucleus of vestibular root; *d*, fibres of descending vestibular root; *n.d.*, a cell of the descending vestibular nucleus; *D.*, cells of nucleus of Deiters; *B*, cells of nucleus of Bechterew; *n.t.*, cells of nucleus tecti (fastigii) of the cerebellum; *p.l.b.*, fibres of the posterior longitudinal bundle. No attempt has been made in this diagram to represent the actual positions of the several nuclei. Thus a large part of Deiters' nucleus lies dorsal to and in the immediate vicinity of the restiform body.

Van Gehuchten states that the nucleus of Bechterew alone receives fibres from the ascending branches and that all the other nuclei (dorsal, descending, and nucleus of Deiters) are furnished with fibres from the descending branches.

The **nucleus of Deiters** is especially characterised by the large size of its cells and by the manner in which they are enveloped as by a basket work by the ramifications of the collaterals in question. From these cells fibres arise which pass to the posterior longitudinal bundles of both sides: in these the fibres bifurcate (Cajal), one branch passing upwards to the oculomotor nucleus and giving off collaterals to the nucleus of the sixth nerve, and the other downwards, eventually reaching the anterior column of the spinal cord (antero-lateral descending tract) and terminating by arborisations amongst the cells of the anterior horn (see p. 417). By means of the collateral fibres which supply the sixth and oculomotor nuclei it is probable that the conjugate movements of the two eyes are brought about. Fibres have also been described as passing from Deiters' nucleus to the nucleus tecti of the cerebellum. Owing to its connections with the semicircular canals, the cerebellum, the oculomotor nuclei, and the nuclei in the anterior horn of the spinal cord, this nucleus has important functions in connection with co-ordination of head and eye movements and equilibration in general.

The fibres which originate in the **nucleus of Bechterew** pass into the reticular formation and become longitudinal, but their destination is not certainly known. Some are said to pass into the anterior column of the cord.

The **reticular formation** still occupies the greater part of each lateral half of the bulb between the grey matter at the floor of the fourth ventricle and the pyramids, and a small portion of the *olivary nucleus* may still be seen, as may also the descending root of the fifth nerve with its adjacent grey matter.

The **restiform body** is formed partly of the fibres of the cerebellar tract of Flechsig of the same side, which are derived below from the cells of Clarke's column, and pass above into the middle lobe of the cerebellum, partly of fibres from the opposite olivary nucleus, and partly of fibres from the olivary nucleus of the same side. The olivary fibres pass mainly to the cerebellar hemisphere. According to some authorities the restiform body contains fibres derived from the nucleus gracilis and nucleus cuneatus of the opposite side. It is said also to receive some fibres from a nucleus which lies just outside the main mass of grey matter of the funiculus cuneatus, and is known as the *outer cuneate nucleus*.

The **floor of the fourth ventricle** is covered by a layer of ciliated epithelium-cells, continuous below with those lining the central canal, and above, through the Sylvian aqueduct, with the epithelium of the third and lateral ventricles. The epithelium rests upon, and its cells assist in forming, a layer of neuroglial tissue known as the *ependyma* of the ventricle. The fourth ventricle is roofed over by a layer of pia mater, with projecting choroid plexuses, the under surface of which is covered by a thin epithelial layer continuous at each side with the ciliated epithelium of the floor. The roof becomes somewhat thickened as it is continued into the ependymal layer of the floor of the ventricle; this thickened part (*tænia* or *ligula*, figs. 532, 533), is often left attached when the thin epithelial roof is removed along with the pia mater which covers it.

LESSONS XLII. AND XLIII.

THE PONS VAROLII, MESENCEPHALON, AND THALAMENCEPHALON.

1. Sections through the lower, middle, and upper parts of the pons Varolii.

2. Sections across the region of the corpora quadrigemina, one at the level of the inferior, the other at the level of the superior, pair.

3. A section across the posterior part of the third ventricle passing through the optic thalami.

In all the above sections sketch under a low power the general arrangement of the grey and white matter, inserting the positions of the chief groups of nerve-cells.

[The tissue is hardened and the sections are prepared, stained, and mounted in the same way as the spinal cord and medulla oblongata.]

THE PONS VAROLII.

Sections through the **lower part of the pons** (fig. 540) show much the same arrangement of grey and white matter as that met with at the upper part of the medulla oblongata, but the general appearance of the sections is much modified by the presence of a large number of transversely coursing bundles of nerve-fibres, most if not all of which are passing to the hemispheres of the cerebellum (fibres of middle peduncle of cerebellum).[1] Intermingled with these bundles is a considerable amount of grey matter (*nuclei pontis*) from the cells of which the fibres of the middle peduncle (of the opposite side) are derived. Amongst the cells of the nuclei pontis many collaterals of the pyramid-tracts end, and the cortico-pontine fibres (see below) also terminate here; thus forming a connection between the cerebral hemisphere of the one side and the opposite cerebellar hemisphere. The continuation of the pyramids of the medulla oblongata (fig. 540, *py*) is imbedded between the transverse bundles of the pons, but the pyramid bundles of the pons are much larger than the pyramids of the medulla oblongata, and, in addition to fibres of the pyramid-tract proper (*cortico-spinal system*), derived from the motor area of the cortex, they are largely composed (especially the postero-lateral bundles) of fibres (*cortico-pontine system*) connecting other regions of the cortex with this part of the hind-brain. The pyramid bundles are separated from the reticular formation by deeper transverse fibres, which belong to a different system from those of the middle peduncle. They form what has already been referred to as the *trapezium* (figs. 538, 540); a collection of fibres which forms part of the central auditory path, and some of which appear to be commissural between the auditory nuclei of the two sides. The fibres of the trapezium traverse a collection of nerve-cells which lies mesial and ventral to the superior olivary nucleus, and is known as the *nucleus of the trapezium* (fig. 538, *n.tr.*).

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[1] Some of the most anterior of these peduncular fibres often form a detached bundle which is known as the *tænia pontis*.

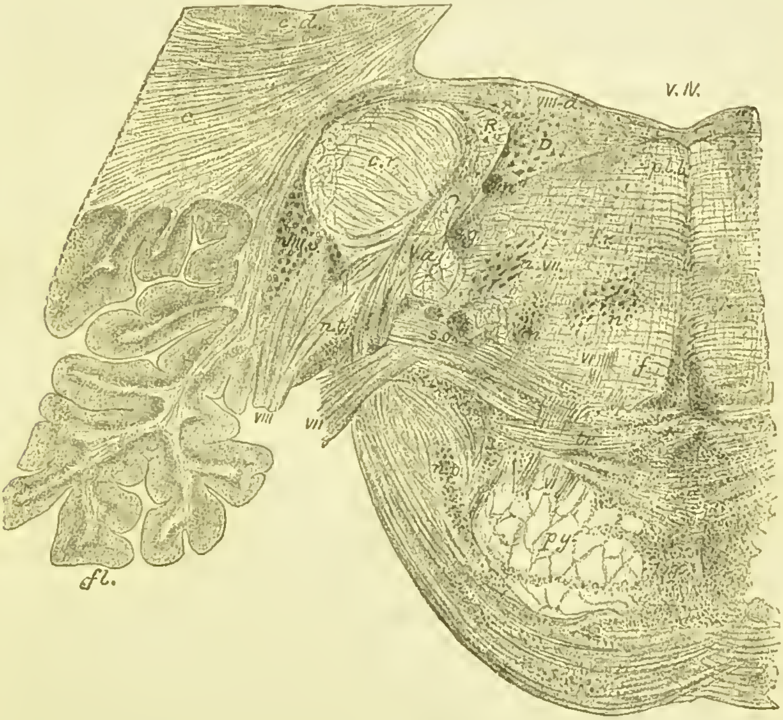

FIG. 540.—TRANSVERSE SECTION THROUGH THE LOWERMOST PART OF THE PONS VAROLII. $\frac{4}{1}$. From a photograph.

v.IV., fourth ventricle; *c*, white matter of cerebellar hemisphere; *c.d.*, corpus dentatum; *fl.*, flocculus; *c.r.*, corpus restiforme; *R*, bundle of Roller, composed of the descending branches of the vestibular nerve; *D*, nucleus of Deiters; *VIII.*, issuing root of auditory nerve; *VIII.d.*, principal or dorsal nucleus of the vestibular nerve; *VIII.v.*, nucleus of cochlear portion; *tr.*, trapezium; *n.tr.*, its nucleus; *f*, fillet; *p.l.b.*, posterior longitudinal bundle; *f.r.*, formatio reticularis; *n*, *n'*, *n''*, various nuclei within it; *V.a.*, descending root of fifth nerve; *s.g.*, substantia gelatinosa; *s.o.*, superior olive; *VII.*, issuing root of facial nerve; *n.VII.*, its nucleus; *VI.*, root-bundles of sixth nerve; *py*, pyramid bundles; *n.p.*, nuclei pontis.

This nucleus is characterised by the peculiar chalice-like synapses (see fig. 207) which the entering axons of the larger acoustic fibres form with the cell-bodies (Held). According to Cajal these large fibres are continued directly from the root-fibres of the cochlear nerve, and are not derived from the cells of its accessory nucleus.

The olivary nucleus is no longer seen, but there are one or two small collections of grey matter, more conspicuous in some animals than in man, which lie in the ventral part of the reticular formation, and are known as the *superior olivary nucleus* (*o.s.*), the *pre-olivary nucleus*, and the *semilunar nucleus* (Cajal). All these, as well as the nucleus of the trapezium itself, are connected with the fibres of the trapezium which form the central auditory path, some of these fibres either ending in the nuclei in question or giving off to them numerous collaterals; whilst from the cells of the nuclei axons pass into the trapezium or into the adjacent lateral part of the fillet. On the other hand, the superior olive is said to receive fibres from the posterior colliculi of the corpora quadrigemina. The *nucleus of Deiters*, which begins to appear in the upper part of the medulla oblongata, where it has been already studied (p. 444), extends into the pons Varolii, where it lies near the floor of the fourth ventricle, a little mesial to the restiform body (*D*, fig. 540). The nerve-fibres connected with its cells pass towards the middle line and enter the *posterior longitudinal bundle*. Here, as already stated, they divide, one branch passing upwards in the bundle and terminating by arborescence chiefly in the opposite oculomotor nucleus: the other branch extending downwards in the medulla oblongata and cord. In the spinal cord they are found in the antero-lateral descending tract; fibres from each nucleus of Deiters occur in both of these tracts (E. H. Fraser). They terminate by arborescence in the anterior horn of the spinal cord.

The nerves which enter or emerge from the grey matter of this region of the brain are part of the *eighth*, the *seventh*, the *sixth*, and somewhat higher up the *fifth* cranial nerves. Of these the eighth (already considered) and fifth are connected with groups of nerve-cells which occupy the grey matter opposite the external border of the floor of the ventricle; the sixth with a nucleus which is also placed in the grey matter of the floor of the ventricle but nearer the middle line, and the seventh with a special nucleus which lies in the formatio reticularis.

The VIIth or facial nerve and the nerve of Wrisberg (pars intermedia).—The motor fibres of the *seventh nerve* arise from the facial nucleus (in the formatio reticularis) which is homologous with the nucleus ambiguus seen in sections of the medulla oblongata. It has been shown that the motor fibres to the stapedius arise from the mesial part of the nucleus and then in succession those of the external ear muscles, those of the mouth and face, and, finally, from a group of cells situated dorsally to the rest, the motor fibres supplied by the superior branch of the nerve (Marinesco, Van Gehuchten). From the nucleus of origin the fibres first pass obliquely backwards to the floor of the ventricle, then longitudinally upwards for a short distance (figs. 534, *A*, 541), and finally bend obliquely forwards and downwards to emerge between the transverse fibres at the side of the pons. None of its fibres are derived from the nucleus of the sixth, as has sometimes been supposed. As it curves over this nucleus it gives off a bundle of fine fibres which cross the raphe, but their destination is unknown. The nucleus of the facial receives collaterals from the adjacent sensory tracts in the formatio reticularis.

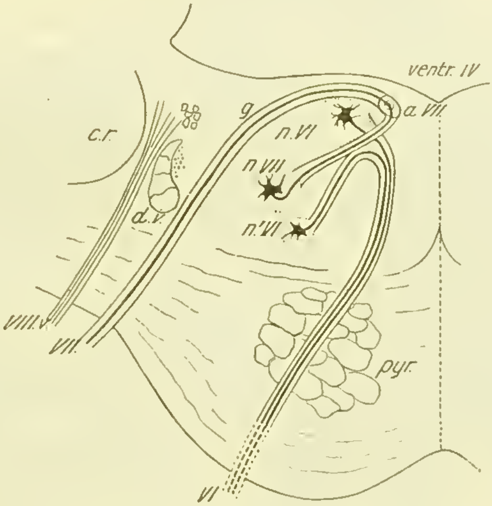

FIG. 541.—PLAN (TRANSVERSE) OF THE ORIGIN OF THE SIXTH AND SEVENTH NERVES.

VI., sixth nerve; *VII.*, seventh nerve; *a.VII.*, ascending part of root of seventh shown cut across near the floor of the fourth ventricle; *g*, genu of seventh; *n.VI.*, chief nucleus of the sixth nerve; *n'.VI.*, accessory nucleus of sixth; ***n.VII.***, nucleus of seventh; ***d.V.***, descending root of fifth; *pyr.*, pyramid bundles; ***VIII.v.***, vestibular root of eighth nerve.

The facial is not a purely motor nerve, but has a ganglion upon it of the spinal type (*geniculate ganglion*) from which fibres arise (fig. 534, *B*) which pass centrally into the pars intermedia of Wrisberg, which enters the pons between the seventh and eighth nerves, and the fibres of which bifurcate into ascending and descending branches like other sensory nerves; the descending branches pass into the solitary bundle and end like those of the glossopharyngeal in the upper part of its accompanying grey matter. The peripheral axons of the cells of the geniculate ganglion pass into the large superficial petrosal and chorda tympani—to which they probably furnish gustatory fibres. Other (efferent) fibres pass into the pars intermedia and ultimately into the chorda tympani from certain large cells which occur in the dorsal part of the facial nucleus. These are probably the salivary and vasodilator fibres of the chorda.

The VIth nerve (abducens).—The fibres of the *sixth nerve* (figs. 534, 541), which are purely motor, pass out from the mesial aspect of the nucleus and turn forwards; traversing the pyramid bundles they emerge at the lower margin of the pons. A few fibres are derived from a small *ventral nucleus* lying near the nucleus of the facial; these run at first backwards and then turn forwards to join the others (Van Gehuchten) (fig. 541, *n'. VI.*).

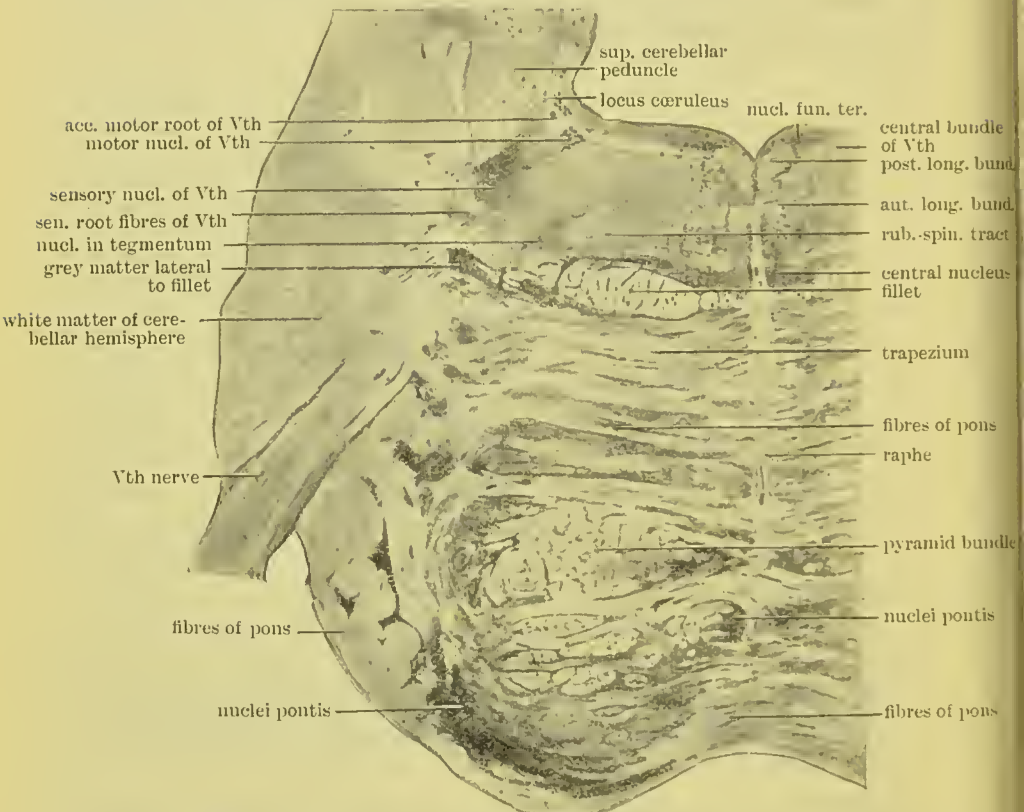

Fig. 542.—Section across the middle of the pons Varolii. Magnified about 4 diameters.

The **Vth** or **trigeminal nerve** emerges at the side of the pons in two roots, a smaller motor and a larger sensory.

The *motor root* is derived partly from fibres which arise in the upper part of the pons and lower part of the mesencephalon from large spherical unipolar nerve-cells lying at the side of the grey matter bounding the Sylvian aqueduct (*accessory* or *superior motor nucleus of fifth*, fig. 534, *n Vms*; fig. 543, *m'n. V.*), partly from the *motor nucleus* *proper* (figs. 534, *nVm*; 543, *mn.V.*) which lies in the grey matter at the lateral edge of the fourth ventricle (fig. 542). As they pass the motor nucleus proper the fibres from the superior or accessory nucleus give off into it a large number of collaterals which ramify between and around its cells.

The fibres of the *sensory root* are derived from the cells of the Gasserian ganglion which are homologous with the cells of the spinal ganglia. These fibres of the sensory root when traced into the pons are found to bifurcate, the ascending branches ending in a mass of grey matter (*principal sensory nucleus of the fifth*, fig. 543, *p.s.n.V.*) lying just lateral to the motor nucleus, while the descending branches trend downwards into the medulla oblongata where they form the descending or spinal root of the fifth (fig. 543, *d.s.V.*); some even reach the upper part of the spinal cord. They lie immediately lateral to and in close connection with the substantia gelatinosa Rolandi

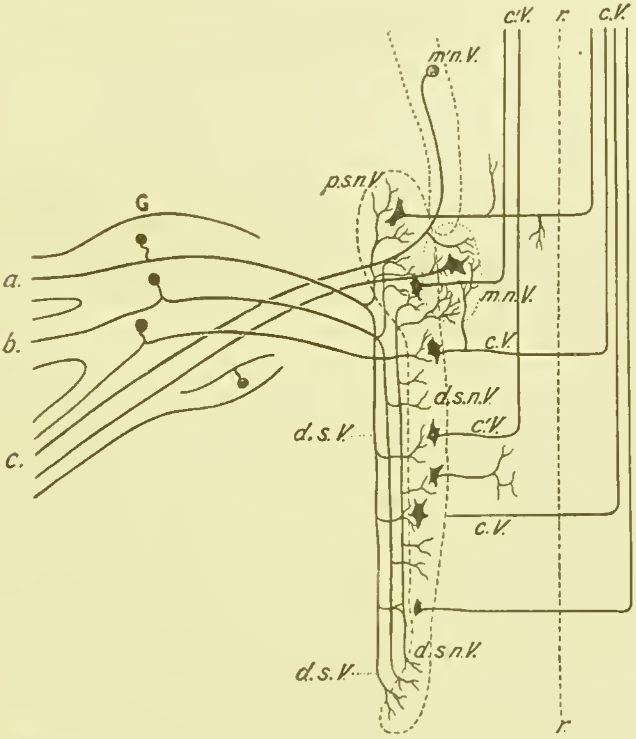

FIG. 543.—PLAN OF THE ORIGIN OF THE FIBRES OF THE FIFTH NERVE.

G, Gasserian ganglion; *a*, *b*, *c*, three divisions of the nerve; *m'.n.V.*, superior motor nucleus; *m.n.V.*, principal motor nucleus; *p.s.n.V.*, principal sensory nucleus; *d.s.n.V.*, descending sensory nucleus; *d.s.V.*, descending root; *c.V.*, *c'.V.*, central sensory tracts composed of fibres emanating from the sensory nuclei; *r*, plane of the raphe.

which forms the *inferior sensory nucleus* (*d.s.n. V.*), and which is continued above into the principal nucleus. The substantia gelatinosa which forms the sensory nucleus of the fifth contains numerous nerve-cells, both small and large; many of the small cells are grouped into nest-like clusters (*islands of Calleja*). The axons of the larger cells pass for the most part across the raphe to the formatio reticularis of the opposite side, where they reinforce the ascending fibres of the intermediate fillet, but some ascend in the fillet of the same side, and others pass to a special *ascending bundle* of fibres on the opposite side of the raphe which lies nearer the floor of the fourth ventricle, and in the tegmentum of the mid-brain lies lateral to the posterior longitudinal bundle; hence it is continued upwards into the thalamus. Collaterals are given off from these ascending fibres to the adjoining grey matter, and especially to the nucleus of the facial nerve. Branches also pass downwards into the formatio reticularis.

Descending tracts in the pons and medulla oblongata.—Besides the *fibres of the pyramids*, which are much more numerous in the pons than in the medulla oblongata, and which send numerous collaterals into the grey matter of the nuclei pontis, there are several other descending tracts of fibres in the pons and medulla oblongata. One of these, which lies mesial to the fillet (see next page), consists of fibres (*cortico-bulbar*) passing from the motor cortex towards the nuclei of the facial and hypoglossal. In the crusta of the mid-brain these fibres lie mesial to the ordinary pyramid fibres, but they then leave the latter and pass into the ventral part of the tegmentum and are continued downwards in the formatio reticularis into the medulla oblongata. Another bundle, consisting of both ascending and descending fibres (*vestibulo-motor*), is very distinct, just ventral to the grey matter of the floor of the fourth ventricle, near the middle line; this is the *dorsal* or *posterior longitudinal bundle*. As already noticed it connects Deiters' nucleus with the oculomotor nucleus, the nucleus of the sixth, and the anterior horn cells of the spinal cord; it probably also receives fibres from the axons of the large cells of the formatio reticularis.

Other descending tracts in the pons which are not so distinctly marked in the normal condition, but which can be traced by the methods of Waller and Flechsig, are:—1. *Monakow's bundle*; 2. *The anterior longitudinal bundle*; 3. *The ponto-spinal lateral tract*; 4. *The vestibulo-spinal tract*; 5. *The central tract of the tegmentum.*

Monakow's bundle or *the rubro-spinal tract* has already been seen as the prepyramidal tract of the spinal cord (p. 417). Its fibres arise from the cells of the red nucleus of the mid-brain of the opposite side, crossing the raphe in Forel's decussation (p. 461, footnote).

In the upper part of the pons it is dorsal to the mesial fillet, but lower down runs in the lateral part of the tegmentum, dorsal to the lateral fillet.

The *anterior longitudinal bundle* (*tecto-spinal tract*) consists of fibres which arise in the opposite superior quadrigeminal body, these cross the raphe in Meynert's decussation (p. 461), and run down ventral to the posterior longitudinal bundle, giving off collaterals to the oculo-motor nuclei and the nuclei of the fourth and sixth nerves as they descend. Its fibres eventually mix with those of the posterior longitudinal bundle, and pass into the anterior column of the cord, joining the antero-lateral descending tract (p. 417).

The *ponto-spinal lateral tract* is formed of fibres which arise from the large cells of the reticular formation, and run down within the lateral area of this formation in the pons and medulla oblongata to reach the part of the lateral column of the cord which lies between the grey matter and the tracts of Monakow and Gowers. It is, however, mixed here with many fibres of different origin. The destination of its fibres is similar to those of the posterior and anterior longitudinal bundles, viz.: the adjacent grey matter of the anterior horn.

The *vestibulo-spinal tract* is composed of fibres derived from the cells of the nuclei of Deiters and Bechterew, and is therefore similar in its origin to the fibres of the posterior longitudinal bundle. The destination is in part also similar, for the fibres pass below into the anterior root zone of the cord and end in the grey matter of the anterior horn, but in their course downwards they lie in the lateral part of the medulla oblongata mixed up with those of Monakow's tract and the ponto-spinal tract, as well as with the ascending fibres of Gowers' tract.

The *central tract of the tegmentum* (Bechterew) runs in the pons exactly in the middle of the reticular formation of the tegmentum, but in the medulla oblongata it lies more ventrally near the olivary nucleus, beyond which it has not been traced. The origin of its fibres is not certainly known, but appears to be the thalamus; their destination is the olivary body of the same side (see p. 435, *thalamo-olivary tract*).

Ascending tracts in the pons and medulla oblongata.—In the ventral part of the reticular formation is a very well-marked tract of fibres somewhat flattened (narrow in section) from above down in the pons; this is the *tract of the fillet.* Its fibres are partly derived from cells in the nuclei of the opposite fasciculus gracilis and fasciculus cuneatus of the medulla oblongata which have crossed the raphe as internal arcuate fibres; partly from cells in the nuclei which are connected with the terminations of the sensory cranial nerves.

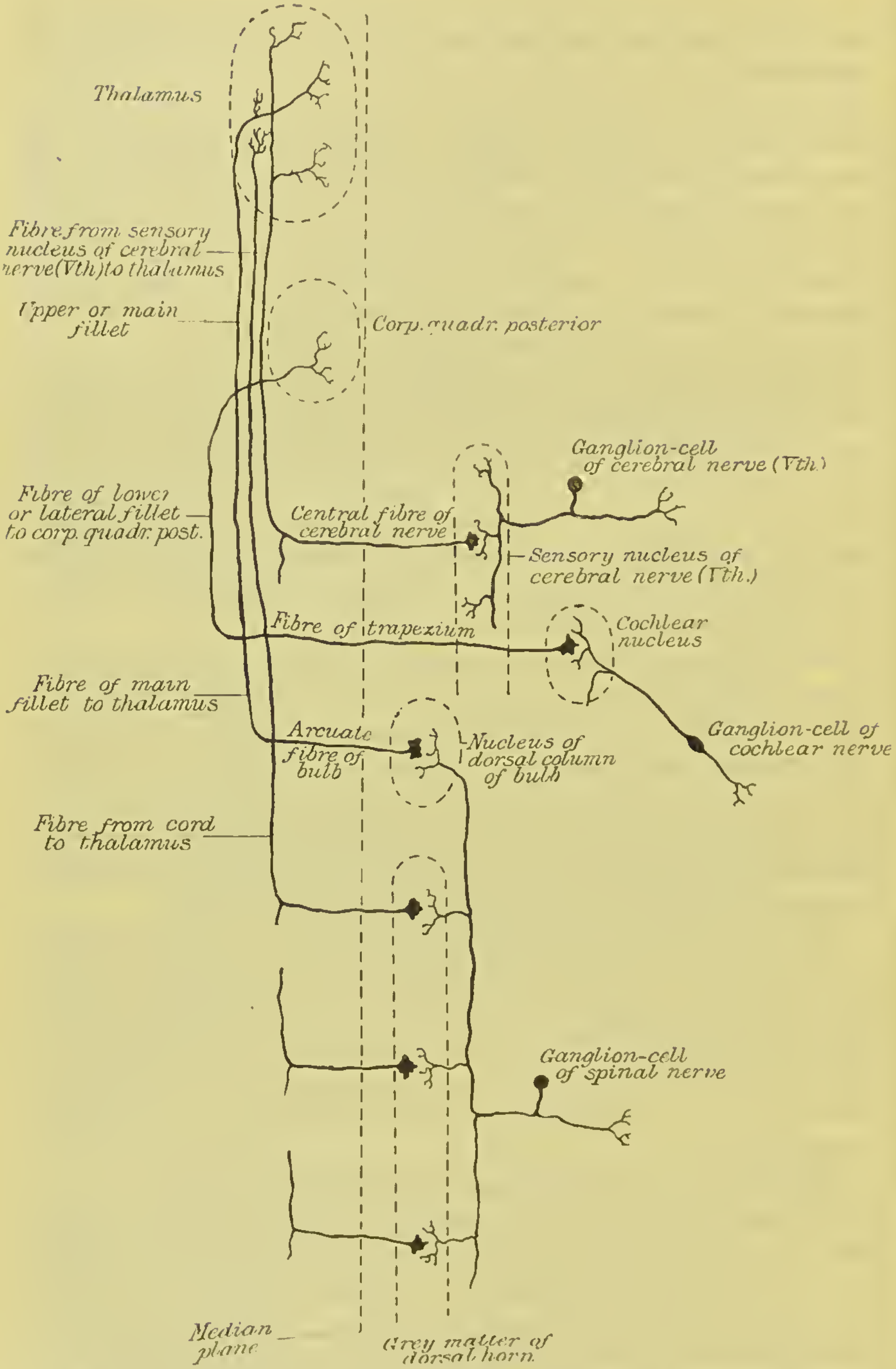
Thalamus
Fibre from sensory nucleus of cerebral nerve (Vth) to thalamus
Upper or main fillet
Corp. quadr. posterior
Ganglion-cell of cerebral nerve (Vth.)
Fibre of lower or lateral fillet to corp. quadr. post.
Central fibre of cerebral nerve
Sensory nucleus of cerebral nerve (Vth.)
Fibre of trapezium
Cochlear nucleus
Fibre of main fillet to thalamus
Arcuate fibre of bulb
Nucleus of dorsal column of bulb
Ganglion-cell of cochlear nerve
Fibre from cord to thalamus
Ganglion-cell of spinal nerve
Median plane
Grey matter of dorsal horn

FIG. 544.—DIAGRAM OF SENSORY PATH TO MID-BRAIN AND THALAMUS.

In the mid-brain the fillet splits up into two distinct bundles of fibres termed respectively the *lateral* or *lower* and the *intermediate* or *upper fillet.* The fibres of the lower fillet are seen at the side of the mesencephalon (*fillet of Reil*), and are traceable partly to the grey matter of the inferior corpora quadrigemina (fig. 551), partly to the mesial geniculate body, in both of which they terminate; they are derived from the sensory nuclei of the medulla oblongata and pons (mainly from the acoustic nuclei). Those of the upper fillet go to the thalamus (fig. 555); they are chiefly the fibres from the cells of the opposite posterior columns of the medulla oblongata.

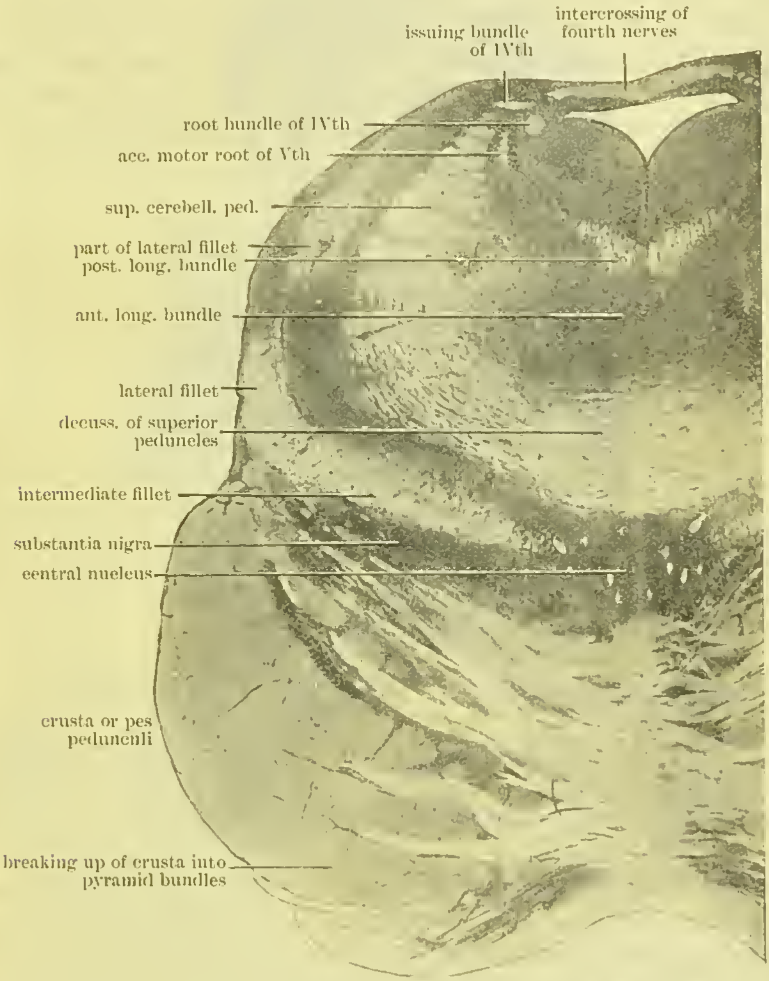

FIG. 545.—TRANSVERSE SECTION THROUGH THE UPPER PART OF THE PONS.

Besides the ascending fibres of the tract of the fillet, this bundle includes a certain number which degenerate below a section of the tract and are therefore descending (centrifugal): their cells of origin appear to lie in the thalamus ; the fibres themselves are situated mesial to the true fillet of which they were formerly considered to be a part (being termed " mesial " fillet) : they form a *thalamo-bulbar tract.* Mesial to the tract just mentioned is a bundle, also consisting of descending fibres belonging to the system of the pyramid-tract, and containing fibres which eventually come into relation with certain of the cranial motor nuclei (Hoche). This constitutes the *cortico-bulbar tract* (see page 452). In the crusta it lies dorso-lateral to the other pyramid-tract fibres.

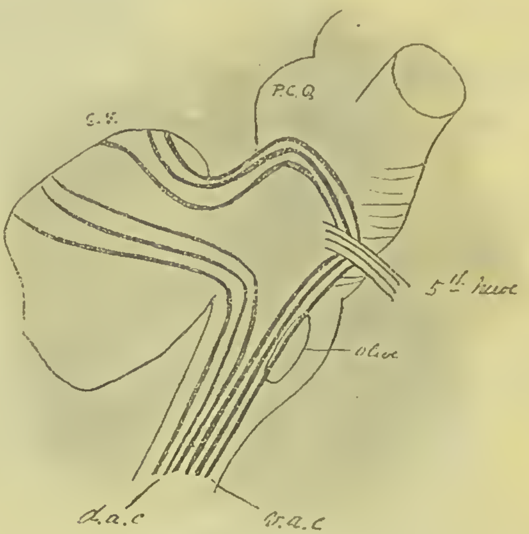

FIG. 546.—DIAGRAM TO SHOW THE MODE OF PASSAGE OF THE FIBRES OF THE DORSAL AND VENTRAL SPINO-CEREBELLAR TRACTS RESPECTIVELY INTO THE CEREBELLAR VERMIS. (F. W. Mott.)

p.c.q., posterior corpora quadrigemina ; *s.v.*, superior vermis of cerebellum : *d.a.c.*, dorsal ascending cerebellar tract ; *v.a.c.*, ventral ascending cerebellar tract.

Many of the fibres which continue the sensory path of the cranial nerves upwards lie in the formatio reticularis (tegmentum), somewhat dorsal to the tract of the fillet, forming a homologous but not clearly defined tract, which runs up through the pons and mid-brain to terminate in the subthalamic region and in the optic thalamus (*central tract of the sensory cranial nerves*). Another ascending tract is the special bundle of fibres from the sensory nucleus of the 5th to the thalamus previously referred to (p. 452).

At the **upper part of the pons** (fig. 545) the fourth ventricle narrows gradually towards the Sylvian aqueduct, and above and on either side of it two considerable masses of longitudinal white fibres make their appearance. These are the *superior peduncles of the cerebellum*, and they tend, as they pass forwards, gradually to approach the

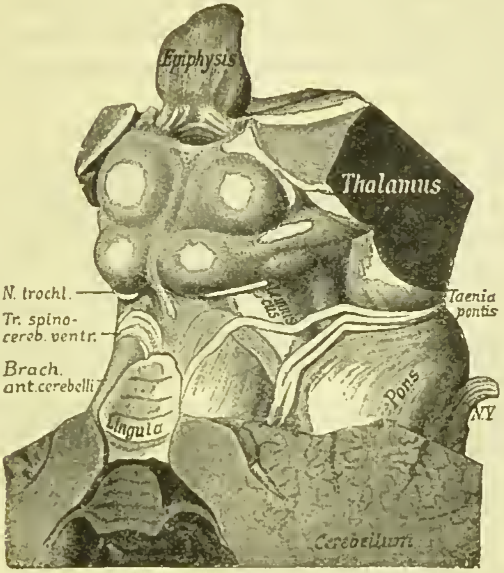

FIG. 547.—THE CORPORA QUADRIGEMINA AND NEIGHBOURING PARTS OF THE BRAIN. (Edinger from G. Retzius.)

Brach. ant. cerebelli, the superior cerebellar peduncles, between them the anterior medullary velum partly covered by the lingula; *Tr. spino-cereb. ventr.*, tract of Gowers curving round the peduncle; *lemniscus*, the lateral fillet; *N. trochl.*, 4th nerve; *N. V.*, 5th nerve.

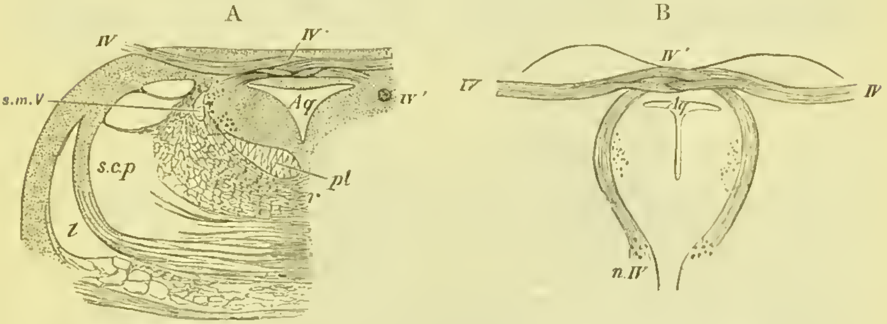

FIG. 548.—SECTION THROUGH THE ORIGIN OF THE FOURTH NERVE. (Schwalbe.)

A, transverse section at the place of emergence of the nerve-fibres. B, oblique section carried along the course of the bundles from the nucleus of origin to the place of emergence. *Aq*, Sylvian aqueduct, with its surrounding grey matter; *IV*, the nerve-bundles emerging; *IV′*, decussation of the nerves of the two sides; *IV″*, a bundle passing by the side of the aqueduct to emerge a little lower down; *n. IV*, nucleus of the fourth nerve; *l*, lateral fillet; *s.c.p*, superior cerebellar peduncle; *s.m. V*, superior motor root of the fifth nerve; *pl*, posterior longitudinal bundle; *r*, raphe.

middle line; across which, immediately below and in the region of the posterior colliculi of the corpora quadrigemina, they pass, decussating with one another, to enter the formatio reticularis of the opposite side.

The fibres of the superior cerebellar peduncles for the most part take origin in the cerebellum, emerging from its dentate nucleus, from the cells of which they are derived. They cross the raphe in the mid-brain and terminate in the red nucleus of the (opposite) tegmentum; but some of them give off a descending branch within the peduncle after crossing: its destination is not known.

The *antero-lateral ascending tract* of the spinal cord (p. 419) is continued up in the lateral column of the medulla oblongata dorso-lateral to the olive and through the ventral part of the pons Varolii lateral to the pyramid bundles, but at about the level of the exit of the fifth nerve many of its fibres begin to pass obliquely towards the dorso-lateral part of the pons (fig. 546), where the superior cerebellar peduncle is emerging from the cerebellar hemisphere. The tract in question (*anterior or ventral spino-cerebellar tract*) now curves over the lateral aspect of this peduncle (fig. 547, *tr. spino-cereb. ventr.*), and then takes a sharp backward turn, passing over its dorsal aspect to enter the middle lobe of the cerebellum in the superior medullary velum.

THE MID-BRAIN OR MESENCEPHALON.

In sections across the **mesencephalon** (figs. 549, 550, 552) the upward continuity of the parts which have already been described in the lower nerve-centres can still in great measure be traced.

The *Sylvian aqueduct* (fig. 550, *Sy*), with its lining of ciliated epithelium, represents the central canal of the cord and the fourth ventricle of the medulla oblongata. In the grey matter which surrounds it (*central grey matter*) there is seen in all sections of the region a group (column) of large nerve-cells (*oculomotor nucleus*) lying ventrally on each side of the middle line, close to the reticular formation. From

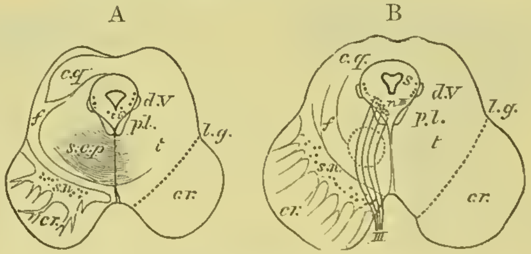

FIG. 549.—OUTLINE OF TWO SECTIONS ACROSS THE MESENCEPHALON. Natural size.

A, through the middle of the inferior corpora quadrigemina. B, through the region of the superior corpora quadrigemina. *cr*, crusta; *s.n.*, substantia nigra; *t*, tegmentum; *s*, Sylvian aqueduct, with its surrounding grey matter; *c.q.*, grey matter of the corpora quadrigemina; *l.g.*, lateral groove; *p.l.*, posterior longitudinal bundle; *d.V.*, superior root of the fifth nerve; *s.c.p.*, superior cerebellar peduncle; *f*, lateral fillet; *III.*, third nerve; *n.III.*, its nucleus. The dotted circle in B indicates the situation of the tegmental or red nucleus.

the lower part of this column the root-bundles of the fourth nerve arise at the lower part of the mesencephalon and pass obliquely backwards and downwards around the central grey matter, decussating with those of the opposite side to emerge just above the pons Varolii (figs. 545, 548). Higher up, in the region of the anterior colliculi, the bundles of the third nerve spring from a continuation of the same nucleus (fig. 552, *n.III.*), and these pass forwards and downwards with a curved course through the reticular formation, to emerge at the mesial side of the crusta. According to Van Gehuchten, some of the fibres of the third nerve cross the middle line and emerge with the nerve of the opposite side.

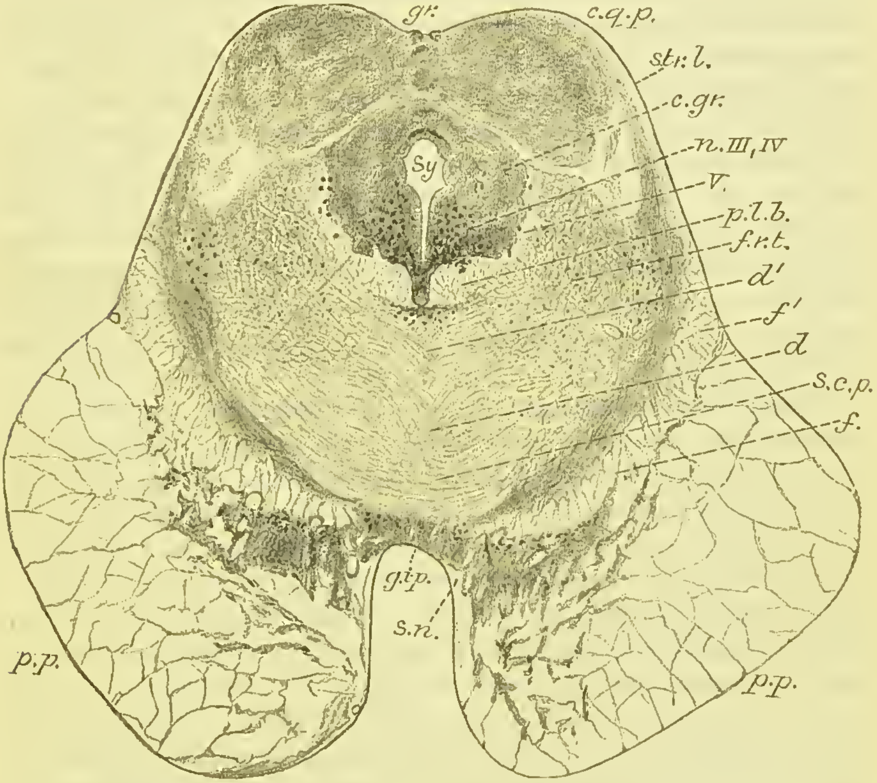

FIG. 550.—SECTION ACROSS THE MID-BRAIN THROUGH THE INFERIOR PAIR OF CORPORA QUADRIGEMINA. Magnified about 3½ diameters. From a photograph.

Sy, aqueduct of Sylvius; *c.gr.*, central grey matter of the aqueduct; *n.III.IV.*, group of cells forming part of the conjoined nucleus of the third and fourth nerves; *c.p.q.*, one of the posterior corpora quadrigemina; *gr*, median groove separating it from that of the opposite side; *str.l.*, stratum lemnisci (layer of the fillet), forming its superficial layer; *f*, upper fillet; *f′*, lateral fillet; V, accessory motor root of fifth nerve; *p.l.b.*, posterior longitudinal bundle; *f.r.t.*, formatio reticularis tegmenti; *d*, *d′*, decussating fibres of tegmenta (fountain-decussations of Forel and Meynert); *s.c.p.*, superior cerebellar peduncles, decussating; *p.p.*, pes pedunculi (crusta); *s.n.*, substantia nigra; *g.i-p.*, interpeduncular ganglion.

Tegmentum.—The reticular formation of the pons is continued up into the mesencephalon and is here known as the *tegmentum.* It is composed as before of longitudinal and transverse or arcuate bundles of fibres with much grey matter intermingled. The transverse fibres include the decussating fibres of the *superior peduncles of the cerebellum* (*s.c.p.*), which are derived from cells in the dentate nucleus of the cerebellum, and on reaching the opposite side bifurcate. Their ascending branches become gradually lost amongst a number of nerve-cells which collectively constitute what is known as the *red nucleus* or *nucleus of the tegmentum*, whilst the descending branches turn downwards in the reticular formation (Cajal) (see p. 458). But some of the fibres of the superior peduncle go on past the red nucleus to the ventral part of the thalamus. The red nucleus also receives fibres in its lateral aspect which are derived from the lenticular nucleus of the corpus striatum, and some of which are said to come from the cerebral cortex; these fibres form a sort of capsule to the red nucleus before entering it.

Tracts in the tegmentum.—1. *Vestibulo-motor tract; posterior longitudinal bundle.*—This is well marked in the mid-brain, and gives off many collaterals and terminal fibres to the oculomotor nucleus which is immediately dorsal to it. The bundle largely consists of nerve-fibres derived from the cells of Deiters' nucleus (see p. 444), which on reaching the situation of the bundle either on the same or on the opposite side, bifurcate, one branch ascending, the other descending. But it receives fibres from other sources than Deiters' nucleus, *e.g.* from large cells of the sensory nucleus of the 5th, and from large cells in the reticular formation of the medulla oblongata, pons, and mid-brain. All these fibres, like those from Deiters' nucleus, bifurcate on joining the bundle, one branch passing upwards, the other downwards. Some fibres of the bundle are of different origin from the rest, arising beyond the oculomotor nucleus. These are very fine; they are descending fibres, and are traceable from the cells of the *nucleus of the posterior longitudinal bundle*, which lies in front of the Sylvian aqueduct in the grey matter at the side of the third ventricle.

Some of the fibres of the posterior longitudinal bundle are stated to be traceable as far up as the thalamus.

The bundle gives collaterals not only to the oculomotor nucleus but also to the nucleus of the sixth, and probably others to the nuclei of other cranial motor nerves. Its descending fibres are eventually continued down the spinal cord in the antero-lateral descending tract, and give off terminals and collaterals to the anterior horn.

2. *Rubro-spinal tract; Monakow's bundle.*—The cells of the red nucleus

send their axons downwards and forwards. They form Monakow's bundle or the *rubro-spinal tract*, which is continued below into the *pre-pyramidal tract* of the spinal cord.

3. *Tecto-spinal tract; anterior longitudinal bundle.*—Other longitudinal fibres of the tegmentum are those of the *fasciculus retroflexus of Meynert* lying mesially to the red nucleus and passing obliquely downwards and inwards from the ganglion of the habenula to the interpeduncular ganglion of the opposite side, and the *bundle of Münzer*, which passes from the posterior tubercle downwards into the lateral part of the reticular formation of the pons. But the longest and most important is the *anterior or ventral longitudinal bundle*, which passes lateral to the red nucleus and partly through it. Although the red nucleus receives many collaterals from this bundle the fibres of the bundle are derived, according to Held and Cajal, from cells in the grey matter of the opposite anterior tubercle of the corpora quadrigemina; these cells send their axons sweeping round the central grey matter just central to the posterior longitudinal bundle to cross in the raphe, where they form the *fountain-like decussation of Meynert* (fig. 550, *d'*).[1] The downward continuation of the tecto-spinal tract has already been studied, but it should be stated that the prolongation of its fibres into the anterior column of the spinal cord is denied by Van Gehuchten, who traces them only as far as the medulla oblongata.

4. *Tract of the fillet.*—The continuation upwards of the fillet is also apparent in this part of the brain. Some of its fibres are seen passing in an oblique manner to the side of the mesencephalon, to enter the grey matter of the prominences of the posterior corpora quadrigemina.

This part is the *lateral fillet* (see p. 455), which is formed chiefly by fibres derived from the accessory auditory, the inferior olivary, and the trapezoid nuclei of the opposite side, forming the *central acoustic tract*. Its fibres send numerous collaterals to the posterior tubercle (fig. 551) and a few to the anterior, and end by ramifying amongst the cells of the mesial geniculate body (Cajal). In its course it traverses the *nucleus of the fillet*, which consists of cells interpolated amongst its fibres (the greater number in the lower part near the superior olive), amongst which some of the fibres and many collaterals from them end. The axons of these cells trend inwards towards the raphe. The *upper fillet* is continued upwards in the ventral part of the tegmentum towards the thalamus (p. 467).

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[1] This is not to be confounded with the *fountain-like decussations of Forel* (fig. 550, *d*), which lies nearer the ventral part of the tegmentum, and is partly formed by the intercrossing of Monakow's bundle and partly by v. Gudden's bundle coming from the corpora mamillaria to end in the tegmentum.

Crusta.—Lateral and ventral to the tegmentum is seen on either side the white mass known as the *crusta* or *pes pedunculi* (figs. 549, *cr.*, 550, 552, *p.p.*). This is formed by longitudinally coursing bundles of fibres lying on the ventral aspect of each half of the mesencephalon, and diverging above into the internal capsule of the cerebral hemisphere.

The fibres of the crusta are continued below into the so-called "pyramid bundles" of the pons—which contain, as we have seen, many more fibres than those of the pyramid-tract. This is also the case with the bundles of the crusta, in which the pyramid-tract proper—composed of fibres emanating from the precentral and paracentral gyri—is confined to the middle three-fifths (which, however, includes many cortico-pontine fibres), whilst the mesial fifth is mainly occupied by fibres passing from the lower frontal region to the pons, carrying impulses to the nuclei of the facial and hypoglossal; and the lateral fifth by fibres the origin and functions of which are not certainly known. But it is probable that these last are connected with the regions of the hemisphere behind the Rolandic fissure, especially, perhaps, with the temporal and occipital regions; and are passing from the pyramidal cells of these parts to end in the nuclei of the pons.

Substantia nigra.—The crusta is separated from the tegmentum by a layer of grey matter containing a number of very deeply pigmented nerve-cells (*substantia nigra*; figs. 550, 552, *s.n.*). The substantia nigra receives many collaterals from the adjacent pyramid bundles of the crusta. The crusta and tegmentum, together with the intervening substantia nigra, constitute the *cerebral peduncle* (*pes* or *crus cerebri*).

Interpeduncular ganglion.—Between the cerebral peduncles, just where they diverge from the mass of transverse fibres of the pons, is seen close to the ventral surface of the brain a small mass of grey matter containing a large number of small nerve-cells with large and irregular dendrons, and axons which are directed dorsally into the tegmentum. This is the *interpeduncular ganglion* (fig. 550, *g.i.p.*). It receives on either side the ending of the *fasciculus retroflexus of Meynert* which comes from the *ganglion of the habenula*, a collection of nerve-cells near the superior and mesial part of the thalamus, close to the commencement of the third ventricle (see fig. 558). These ganglia are both much better marked in many of the lower animals than in man.

Corpora quadrigemina.—The prominences (*colliculi* or *tubercles*) of the corpora quadrigemina are formed mainly of grey matter. Connected with each one is a bundle of white fibres forming the *brachia* of the geniculate bodies.

The **posterior or inferior colliculi** consist of a *grey centre* which is enclosed by *superficial* and *deep white layers* (figs. 550, 551). The superficial white layer is derived mainly from the brachium. The fibres of the fillet divide as they approach the colliculus; one branch enters its grey matter while the other passes to the mesial geniculate body. In animals with a highly developed sense of hearing all these parts are proportionately well-developed. The deep white layer is derived from cells of the grey centre, but many of the cells of the latter send their axons towards the superficial layer. The destination of the fibres of

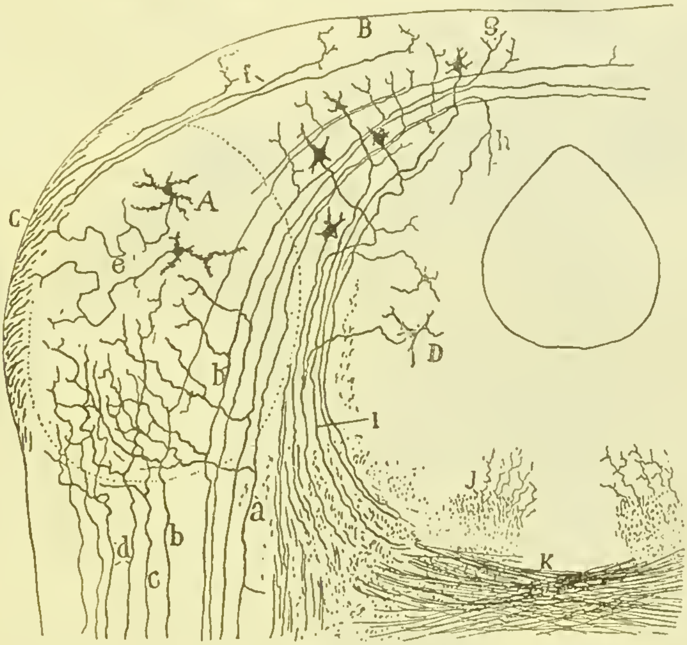

FIG. 551.—DIAGRAM SHOWING THE GENERAL STRUCTURE OF THE POSTERIOR CORPORA QUADRIGEMINA. (Cajal.)

A, principal mass of grey matter; B, C, cortical layer; D, grey matter around Sylvian aqueduct; K, decussation of superior peduncles of cerebellum; *a*, *b*, *c*, *d*, fibres of central acoustic path from lateral fillet; *e*, axons from cells of principal nucleus passing towards brachium; *f*, fibres from brachium passing into superficial layer; *g*, fibres from fillet passing into superficial layer; *h*, a fibre of fillet passing to central grey matter of aqueduct; *j*, collaterals from posterior longitudinal bundle passing to oculo-motor nucleus; *l*, axons of cells in superomesial part of colliculus curving round grey matter of aqueduct and forming the deep white layer.

the deep white layer is not certainly known; some pass over the central grey matter of the aqueduct to the opposite side.

In the **anterior or superior colliculi** four layers can be distinguished, viz.: superficially, a *thin white layer* containing nerve-fibres and a few horizontally disposed nerve-cells (fig. 553, A); next to this a *grey cap* (B) containing many and various nerve-cells, amongst which the terminations of the optic nerve (*h*, *h*) ramify; below this the *optic nerve layer* (C), which is formed of antero-posteriorly running fibres derived from the optic tract, and ending as just stated for the most part in the grey layer. This layer also contains some nerve-cells. Lastly there is a deep white layer, the so-called *deep medulla*, of transversely disposed fibres (D) derived partly from the fillet, but comprising many fibres which are derived from the cells of the colliculus itself, and a few which are continued up from the antero-lateral ascending tract of the spinal cord. This deep layer also contains a number of large dendritic cells amongst the fibres. The superior corpora quadrigemina receive through their brachia many of the fibres of the optic tract, which in mammals enter the grey matter at the middle of its thickness and traverse it from before back, so that in transverse sections of the mid-brain they appear cut across. In birds they form a superficial white stratum covering the grey matter, but this is not homologous with the superficial stratum of mammals, for the fibres in the latter are not

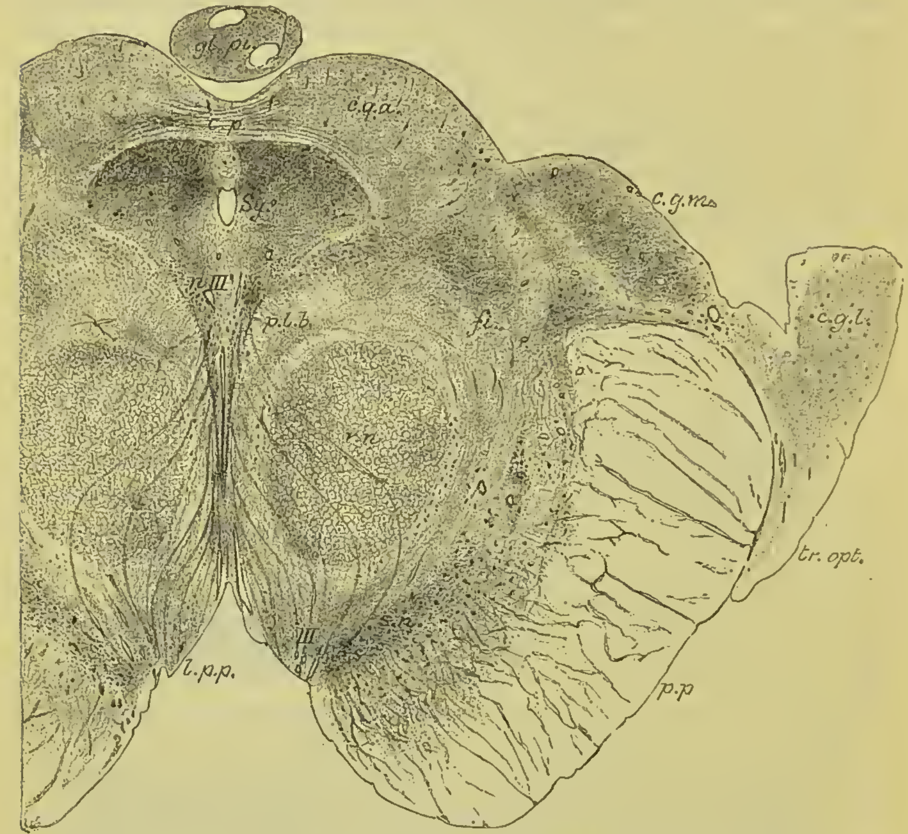

FIG. 552.—SECTION ACROSS THE MID-BRAIN THROUGH THE SUPERIOR CORPORA QUADRIGEMINA. Magnified about 3½ diameters. From a photograph.

c.p., posterior commissure of brain; *gl.pi.*, pineal gland; *c.q.a.*, grey matter of one of superior corpora quadrigemina; *c.g.m.*, mesial geniculate body; *c.g.l.*, lateral geniculate body; *tr. opt.*, optic tract; *p.p.*, crusta or pes pedunculi; *p.l.b.*, posterior longitudinal bundle; *fi*, upper fillet; *r.n.*, red nucleus; *III.*, issuing fibres of third nerve; *n.III.*, its nucleus; *l.p.p.*, locus perforatus posticus; *Sy*, Sylvian aqueduct.

derived directly from the optic tract. The optic fibres are derived from nerve-cells in the retina, and as they traverse the stratum opticum they pass obliquely into the grey matter (in a ventral direction in birds, in a dorsal direction in mammals) and end in arborisations amongst its cells. The cells of the grey matter are very various in form and size (fig. 553). Most of their axis-cylinder processes pass ventralwards. The destination of all is not certainly known, but many appear to join the anterior longitudinal bundle of the opposite side. Others run down on the same side towards the pons Varolii, intermingled with the ascending fibres of the fillet. A certain number of fibres which take origin in the cells of the anterior colliculi course over the central grey matter which surrounds the Sylvian aqueduct and sweep round this towards the fillet-tract of the opposite side. These *commissural fibres* are continuous in front with those of the posterior commissure.

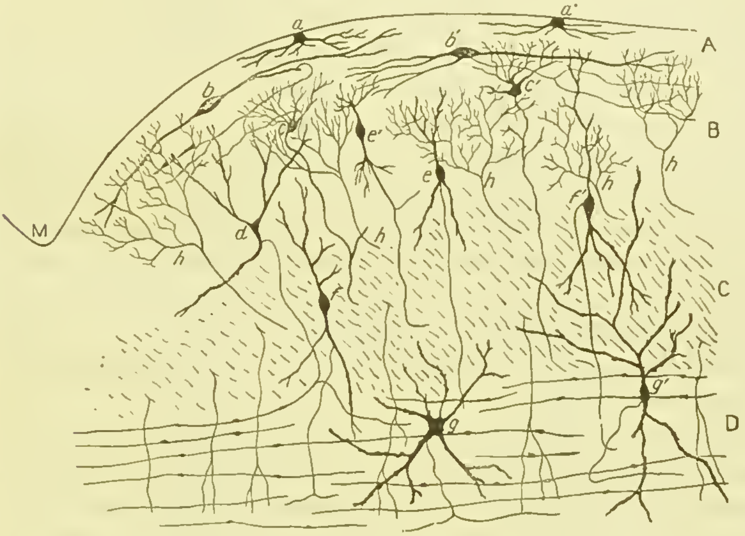

FIG. 553.—DIAGRAM SHOWING THE CHARACTERS OF THE CELLS IN THE GREY MATTER OF THE ANTERIOR CORPORA QUADRIGEMINA. (Cajal.)

M, portion of dorsal median groove; *A*, superficial white layer; *B*, grey cap; *C*, optic fibre layer (upper grey-white layer); *D*, layer of the fillet (lower grey-white layer).

a, *a'*, marginal nerve-cells: their axons are not represented; *b*, *b'*, horizontal spindle-shaped cells of Golgi's type II.; *c*, *c'*, small cells with much branched dendrons and an axon extending to the optic fibre layer; *d*, *e*, *e'*, spindle and stellate cells of the grey cap, and *f*, *f'*, cells of the stratum opticum, sending their axons into the stratum lemnisci; *g*, *g'*, cells of the stratum lemnisci; *h*, *h* fibres of the optic nerve layer ending in the grey and superficial white layers.

The nerve-fibres of the optic nerve and optic tract do not all enter the corpora quadrigemina. Many, indeed the majority, pass into the lateral geniculate bodies and optic thalami to form arborisations there (fig. 557). On the other hand, axons from the cells of these structures pass to the cortex of the brain (occipital region).

As has just been stated, many arcuate fibres issue from the grey matter of the corpora quadrigemina and pass obliquely downwards into the ventral part of the mesencephalon encircling the central grey matter. These fibres intercross in the raphe, where they constitute the fountain-decussation of Meynert (p. 461), and after crossing constitute the main mass of the anterior longitudinal bundles. These are continued into the anterior columns of the spinal cord; they give off collaterals to the motor-nuclei of the eye-muscles, and probably to the motor nuclei generally. Other fibres which appear to belong to the same (*tecto-spinal*) system are traceable as a distinct tract into the lateral column of the cord (see p. 417).

In the cat, the anterior corpora quadrigemina receive a number of fibres from the pyramid-tract in the crusta of the same side, a few crossing over the aqueduct to the opposite corpora quadrigemina (Boyce, Sutherland Simpson). But in most animals the fibres which pass from the cortex cerebri to the corpora quadrigemina enter those bodies through their respective brachia.

No fibres are given off from the cells of the corpora quadrigemina to the cortex cerebri.

The optic nerves.—The only sensory nerves which are immediately connected with the mid-brain are the *second* or *optic*. Their origin is from the large nerve-cells of the ganglion of the retina (p. 515). The nerve leaves the globe of the eye at its posterior aspect, passes through the optic foramen to the base of the brain, and joins the nerve of the opposite side to form the *optic chiasma* (fig. 557). Of the fibres which enter the chiasma, those from the inner (or nasal) two-thirds of the retina cross to the optic tract of the opposite side, while the remaining third, comprising the fibres from the temporal part of the retina, pass along the lateral border of the chiasma to the tract of the same side. In the optic tract they are continued to the parts of the brain where they have their terminal arborescences, viz., the external geniculate body and the adjoining posterior part of the thalamus (pulvinar) and the anterior corpora quadrigemina. A certain number of the fibres of the optic nerve bifurcate on reaching the chiasma, and the branches pass one into each optic tract (Cajal).

The fibres which pass to the anterior corpora quadrigemina are much finer than those to the corpora geniculata. It is probable that the former furnish the path for reflex movements of the pupil, etc., and the latter the path for visual impressions, since the lateral corpora geniculata and pulvinar thalami are directly connected with the visual cortex in the occipital lobe, while, as already stated, no such direct connection obtains between that cortex and the anterior corpora quadrigemina.

A small bundle of fibres (*transverse peduncular bundle*) leaves the optic tract as it enters the mid-brain and passes round the cerebral peduncle to lose itself in the mesial part of the tegmentum near the fillet. Its destination appears to be a small nucleus situated near the red nucleus. Its fibres degenerate after enucleation of the opposite eyeball.

The optic tracts and chiasma also contain the fibres of *v. Gudden's commissure*, which connects the posterior corpora quadrigemina, but these fibres appear to have no relation to the visual function.

There are present in the optic nerve and tract a few fibres which originate in the nerve centres—where is not known—and terminate in the retina.

Motor nerves.—The motor nerves arising from the mid-brain are the third and fourth. The position of their nuclei and their mode of exit have been already described (pp. 458, 459).

Posterior commissure.—Immediately in front of the corpora quadrigemina, visible in the roof of this part of the mid-brain, is the *posterior commissure.* This consists of fibres which arise in a nucleus at each side of the Sylvian aqueduct and which pass across the middle line dorsal to the central grey matter and then turn ventralwards and caudalwards to pass down in the tegmentum lateral to the posterior longitudinal bundle, which is partly reinforced by the fibres in question. The posterior commissure extends into the region of the third ventricle.

THE THALAMENCEPHALON.

The **optic thalamus** (fig. 554, *th.*), which lies at the side of the third ventricle and forms part of the floor of the lateral ventricle, is covered externally by a layer of white fibres, most marked next to the internal capsule. Fibres from the latter pass into the thalamus and serve to connect it with the hemisphere.

The grey matter of the thalamus is partially subdivided by an oblique white lamina into a smaller, *mesial nucleus*, and a larger *lateral nucleus*; these contain a large number of small nerve-cells. Anteriorly another portion of grey matter (*anterior nucleus*) is divided off in a similar way; this contains comparatively large nerve-cells. These nuclei are themselves formed of several groups of cells having different connections, many of which still require elucidation.

The thalamus receives the terminal branches of the fibres of the *upper fillet*, continued from the cells of the opposite nuclei of Goll and Burdach (spino-thalamic tract), of the *central path of the fifth cranial nerve* of the opposite side, and some fibres from the *superior cerebellar peduncle* of the opposite side; besides the fibres of the optic tract which pass to the external geniculate body and pulvinar thalami.

From the cells of the thalamus nerve-fibres pass in every direction into the white matter of the hemisphere, and eventually to the cortex (figs. 520, 555). From the outer part they tend especially in the occipital region, assisting to form the central visual tract which passes to the visual cortex. From the inner and deeper part they converge towards the subthalamic region and many are collected into the ansa lenticularis (see p. 472), by which they pass into the nucleus lenticularis, while others, as already stated, enter the corona radiata and thus reach the cortex of the hemisphere. These fibres from the thalamus to

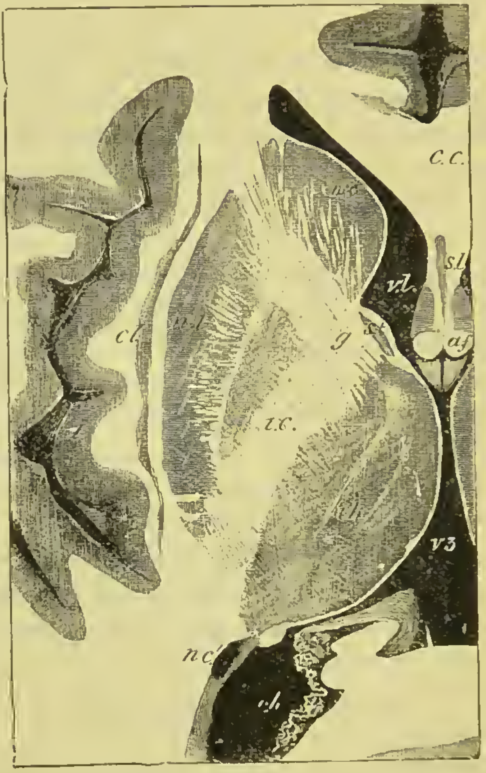

FIG. 554.—HORIZONTAL SECTION THROUGH THE OPTIC THALAMUS AND CORPUS STRIATUM. Natural size.

v.l., lateral ventricle, its anterior cornu; *c.c.*, corpus callosum; *s.l.*, septum lucidum; *a.f.*, anterior pillars of the fornix; *v3*, third ventricle; *th.*, thalamus opticus; *st.*, stria medullaris; *nc.*, *nc'.*, nucleus caudatus, and *nl.*, nucleus lenticularis of the corpus striatum; *i.c.*, internal capsule; *g*, its angle or genu; *nc'.*, tail of the nucleus caudatus appearing in the descending cornu of the lateral ventricle; *cl.*, claustrum; *I*, island of Reil.

the cortex probably form the third and the last link in the chain of sensory neurones, the second being formed by the neurones of the fillet and the first by the neurones of the sensory roots. On the other hand, the thalamus receives fibres from the cortex and from the corpus striatum, which end amongst its cells.

Attached to the optic thalamus below and behind are the *mesial and lateral geniculate bodies* (fig. 556) which at first sight appear to be both

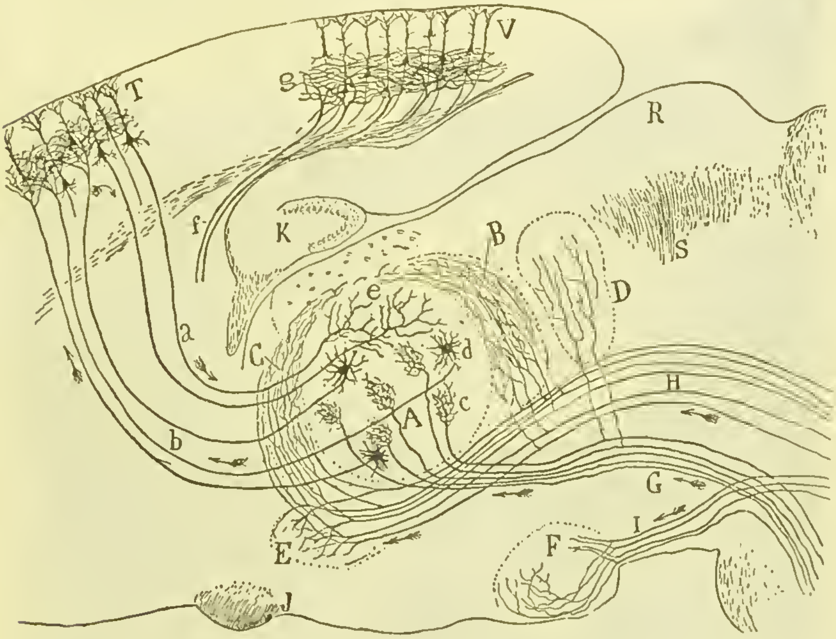

FIG. 555.—DIAGRAM OF THE CONNECTIONS OF THE THALAMUS WITH THE ASCENDING FIBRES OF THE 5TH NERVE, AND OF THE UPPER FILLET ON THE ONE HAND, AND WITH THE CORTEX CEREBRI ON THE OTHER. (Cajal.)

A, B, C, D, E, various nuclei in thalamus; I, afferent fibres passing to mamillary body F; G, tract of upper fillet ending in A (at *c*), and giving collaterals to D (posterior nucleus); H, central tract from sensory nucleus of 5th; T, cortex cerebri; V, visual cortex; R, anterior colliculus; J, optic chiasma; S, optic fibres; K, hippocampus.

a, fibres from cortex to thalamus, ending at *e*; *b*, fibres from cells in thalamus (*d*) to cortex; *f*, fibres from lateral geniculate body and thalamus to visual cortex, ending at *g* in stria of Gennari.

connected with the optic tract, although only the outer one actually receives optic fibres. The inner or mesial geniculate body receives fibres from the central auditory tract through the lateral fillet. Of the geniculate bodies the outer or lateral has a lamellated structure consisting of alternating layers of grey and white matter, the white layers being composed partly of the entering optic fibres and partly of fibres emerging from the grey matter and passing to the central optic path, while the grey substance contains very numerous nerve-cells amongst which the fibres of the optic tract end in complex arborisations. From these cells axons arise and join a bundle of fibres which enters the white matter of the hemisphere above and along with the internal capsule, and passes to the visual area of the cortex (central visual tract). Some of the fibres from the corpus geniculatum laterale, as they enter the visual tract, send branches downwards towards the tegmentum.

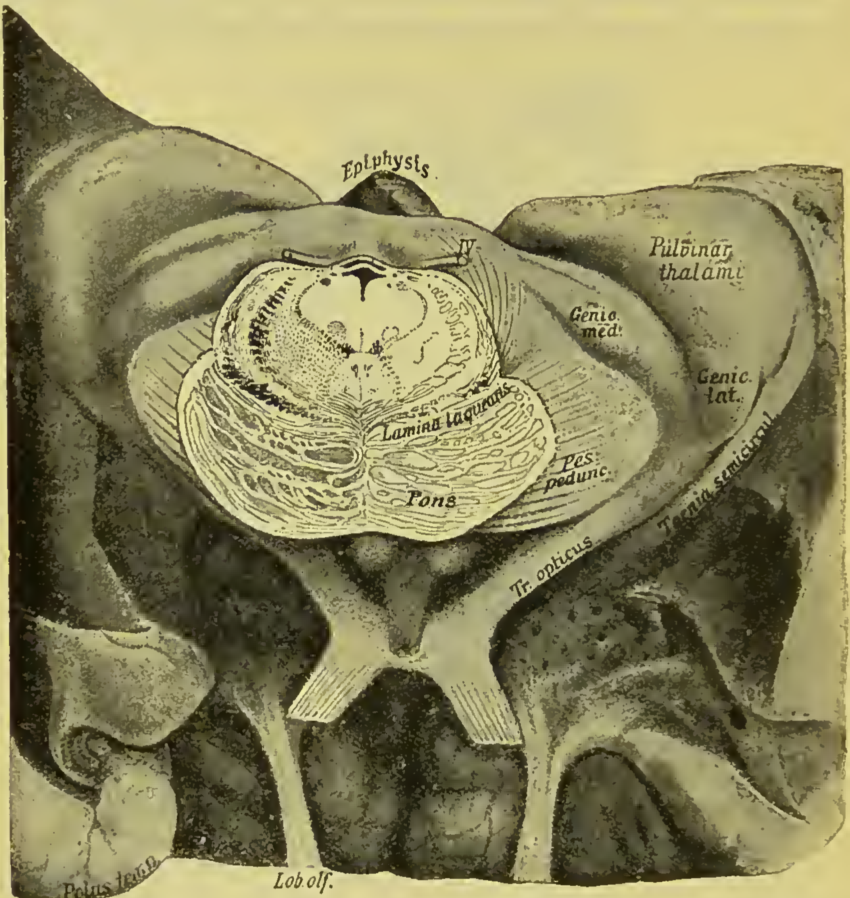

FIG. 556.—FIGURE SHOWING THE OLFACTORY TRACTS AND THEIR ROOTS: THE OPTIC CHIASMA AND OPTIC TRACTS: THE GENICULATE BODIES AND THE PULVINAR THALAMI. (Edinger.)

The pons is cut through at the anterior part, and the section shows the Sylvian aqueduct, the fillet (*lamina laquearis*), superior cerebellar peduncles, etc. (see fig. 545). The corpora mamillaria are partly concealed by the pons; between and in front of them is seen the infundibulum and pituitary body.

The **ganglion of the habenula** (fig. 558, *g′*) is a collection of nerve-cells which lies at the posterior part of the thalamus on each side, near the roof of the third ventricle. This ganglion receives on the one hand the fibres of the *habenula* or *stria medullaris*, and on the other hand gives off from its cells the fibres which form the *fasciculus retroflexus* (fig. 583), which pass downwards to the interpeduncular ganglion (p. 462). The two ganglia of the habenulæ are joined by a white commissure.

The **corpora mamillaria** (fig. 556) are seen at the base of the brain immediately below the posterior part of the third ventricle. Each is composed of white matter externally and grey matter internally. It receives fibres from the anterior pillar of the fornix of the same side; these fibres arise from cells in the hippocampus and end in the mamillary body. According to Edinger some fibres from the olfactory tract pass directly to it. The axons of its cells bifurcate, one branch, the coarser, passing into the anterior and upper part of the thalamus in the bundle of Vicq d'Azyr, and the other into the tegmentum of the mid-brain in v. Gudden's bundle. The corpora mamillaria form part of the central olfactory apparatus (fig. 583).

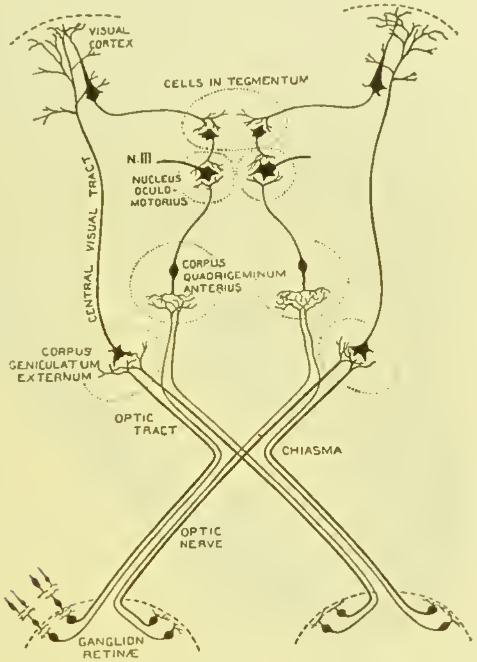

FIG. 557.—DIAGRAM TO SHOW THE PROBABLE COURSE AND RELATIONS OF THE OPTIC FIBRES.[1]

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[1] Only single fibres are shown emerging from the anterior quadrigeminal and external geniculate bodies, continuing the course of the two fibres from corresponding points in the retinæ. This is merely to simplify the diagram, and is not intended to imply that the retinal impressions are fused in those situations.

Subthalamic region.—The tegmentum of the crus cerebri is prolonged below the thalamus opticus, and between it and the internal capsule, into a mass of grey substance, with longitudinally and obliquely crossing white bundles, which is known under the name of *hypothalamus* (fig. 558). Its deepest part contains a lens-shaped mass of grey matter prolonged forwards from the substantia nigra known as the *corpus subthalamicum* (Luys). A mass of fibres sweeps round this and round the internal capsule, passing between the thalamus and the nucleus lenticularis, this is known as the *ansa lenticularis*.

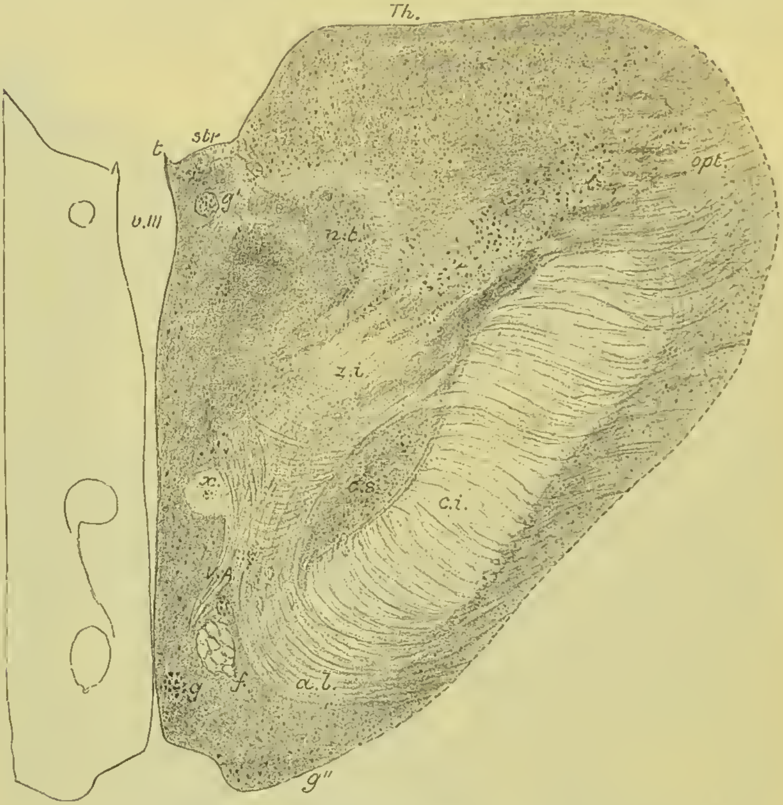


FIG. 558.—SECTION TAKEN OBLIQUELY THROUGH THE OPTIC THALAMUS AND INTERNAL CAPSULE SHOWING SOME OF THE STRANDS OF FIBRES OF THE HYPOTHALAMUS. Magnified $2\frac{1}{2}$ diameters.

Th., thalamus; *v.iii.*, third ventricle; *t.*, tænia, or attachment of epithelial roof of ventricle; *str.*, stria medullaris or habenula; *g'*, ganglion of the habenula; *n.t.*, mesial nucleus of thalamus; *opt.*, optic fibres passing into pulvinar of thalamus; *z.i.*, zona incerta, from which fibres are seen emerging and sweeping as the *ansa lenticularis*, *a.l.*, round the internal capsule, *c.i.*, to pass toward the lenticular nucleus; *c.s.*, corpus subthalamicum; *f.*, anterior pillar of fornix passing backwards to corpus mamillare; *V.A.*, bundle of Vicq d'Azyr, passing upwards and forwards from corpus mamillare into thalamus; *g*, group of nerve-cells, probably belonging to the nucleus of the corpus mamillare; *x*, fasciculus retroflexus.

The **pineal gland** or *epiphysis cerebri* (fig. 552), which is developed in the roof of the third ventricle, but passes backward between the anterior corpora quadrigemina, is composed of a number of tubes and saccules lined and sometimes almost filled with epithelium, and containing deposits of earthy salts (*brain sand*). (Similar deposits may also occur in other parts of the brain, especially in the pia-mater.) The follicles are separated from one another by vascular connective tissue derived from the pia-mater, and along with the vessels are numerous nerve-fibres of sympathetic type (Cajal). No true nerve-cells can be seen, although there are a number of cells similar in general appearance to the "granules" of the cerebellum, but apparently without axons. In some animals (ox) striated muscular fibres have been met with.

In the chameleon and some other reptiles, the pineal is better developed, and is connected by nerve-fibres with a rudimentary median eye of invertebrate type, placed upon the upper surface of the head.

The **pituitary body or gland** (*hypophysis cerebri*) is connected with the third ventricle by the infundibulum. It consists of two lobes, a large anterior and a smaller posterior. The structure of this body has already been described (pp. 254 to 258).

LESSONS XLIV. AND XLV.

STRUCTURE OF THE CEREBELLUM AND CEREBRUM.

1. Sections of the cerebellum vertical to the surface, (*a*) across the direction of the laminæ, (*b*) parallel with the laminæ.

2. Sections across the whole of one hemisphere of the cerebrum of a monkey passing through the third ventricle.

3. Vertical sections of the cerebral cortex:—one across the central gyri, another from the occipital lobe (calcarine region), another across the superior temporal gyrus and island of Reil, and one across the hippocampal gyrus and hippocampus.

4. Transverse sections of the olfactory tract and bulb.

In all these preparations make sketches under a low power of the general arrangement of the grey and white matter, and also of the nerve-cells in the grey matter. Sketch some of the details under a high power.

The preparations are made in the same way as those of the spinal cord. Other preparations may be made by the Golgi or Cox methods to exhibit the relation of the cells to one another. Such preparations have been already partly studied (Lessons XVII. and XVIII.).

The Cerebellum.

The **cerebellum** is composed of a white centre and of a grey cortex. Both extend into all the folds or laminæ, so that when the laminæ are cut across, an appearance is presented of a white arborescence covered superficially by grey matter. The white matter is in largest amount in the middle of each cerebellar hemisphere. There is here present a peculiar wavy lamina of grey matter, similar to that in the olivary body, and known as the *nucleus dentatus* (fig. 559, *n.d.*). This receives numerous nerve-fibres from the cells of Purkinje of the cortex, which end by arborising around its cells. The latter give off axons which become the fibres of the superior cerebellar peduncles, and for the most part end in the opposite red nucleus, but some pass beyond this into the subthalamic region. The dentate nucleus also receives collaterals from fibres of the inferior peduncle (Cajal).

Other isolated grey nuclei lie in the white matter of the middle lobe over the roof of the 4th ventricle and constitute collectively the *nuclei of Stilling*. The most important of these appears to be the *nucleus tecti* (*s. fastigii*) (fig. 559). This receives many of the ascending fibres of the vestibular nerve (p. 443) and collaterals from the spino-cerebellar tracts, and gives origin to a bundle of fibres which crosses to the opposite side and descends in the mesial part of the restiform body to the reticular formation of the medulla oblongata (Risien Russell).

The **grey matter** of the cerebellum appears essentially of similar structure throughout the whole extent of the cortex. It consists of two layers. The *inner* one (that next to the white centre) is composed of a large number of very small nerve-cells intermingled with a few larger ones and some neuroglia-cells (*granule layer*, fig. 560, *d*). The *outer one* is thicker, and is formed chiefly of fine nerve-fibres (fig. 562, *A*) with small nerve-cells scattered through it (*molecular layer*, fig. 560, *b*). Into its outer part processes of the pia-mater conveying blood-vessels pass vertically. Lying between the two layers of the grey matter is an incomplete stratum of large flask-shaped cells (fig. 560, *c*) (*cells of Purkinje*, fig. 561). Each of these gives off from its base a fine process (axon), which becomes the axis-cylinder of one of the medullated fibres of the white centre, while from the opposite pole of the cell large ramified processes (dendrons) extend into the superficial layer of the grey matter.

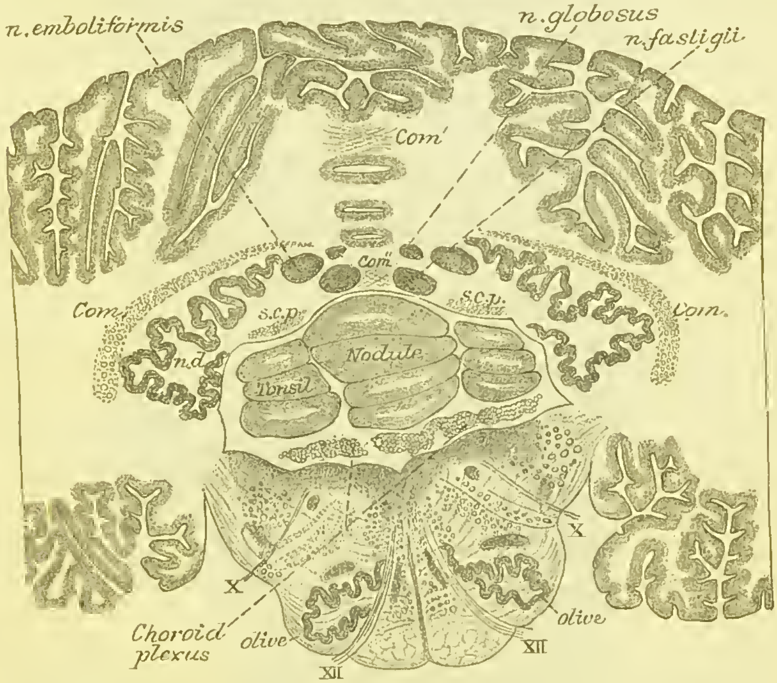


FIG. 559.—SECTION ACROSS THE CEREBELLUM AND MEDULLA OBLONGATA SHOWING THE POSITION OF THE NUCLEI IN THE WHITE CENTRE OF THE CEREBELLUM. (Stilling.)

n.d., nucleus dentatus cerebelli; *s.c.p.*, fibres of superior peduncle; *com, com', com''*, commissural fibres; *X*, rootlet of vagus; *XII*, rootlet of hypoglossal nerve.

The dendrons of the cells of Purkinje spread out in planes transverse to the direction of the lamellæ of the organ, so that they present a different appearance according to whether the section is taken across the lamellæ or along them (compare figs. 562 and 563).

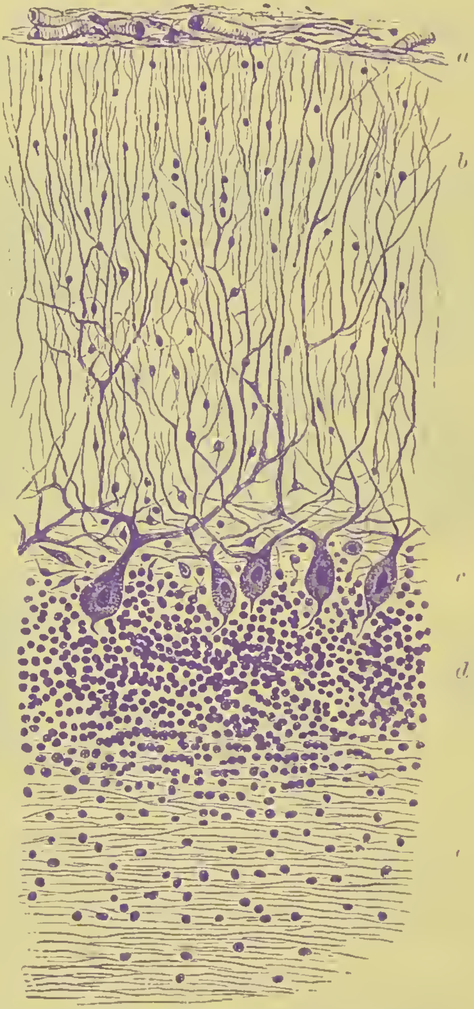


FIG. 560.—SECTION OF CORTEX OF CEREBELLUM. (Sankey.)

a, pia-mater; *b*, external layer; *c*, layer of corpuscles of Purkinje; *d*, inner or granule layer; *e*, medullary centre.

These dendrons are invested at their attachment to the cell, and for some extent along their branchings, by basket-works formed by the terminal arborisations of certain fibres (*climbing or tendril fibres*) of the medullary centre (fig. 565; fig. 566, *cl.f.*). The body of the cell of Purkinje is further invested by a felt-work of fibrils formed by the arborisation of axis-cylinder processes of nerve cells (*basket cells*) in the outer layer of the grey matter (figs. 564; 566, *b*). Each cell has therefore a double investment of this nature, one covering the dendrons, the other the body of the cell and extending along the commencement of the axon.

The *granules* of the inner layer of grey matter are mostly small nerve-cells, each with a few dendrons penetrating amongst the other granules, and an axon which is directed between the cells of Purkinje into the outer layer. After penetrating a variable distance into this layer it bifurcates, and its two branches pass in opposite directions at right angles to the main stem, and parallel to the direction of the lamella (fig. 562). What ultimately becomes of the branches is not known. In sections cut across the lamella the cut ends of these fibres give a finely punctated appearance to the outer layer (fig. 563).

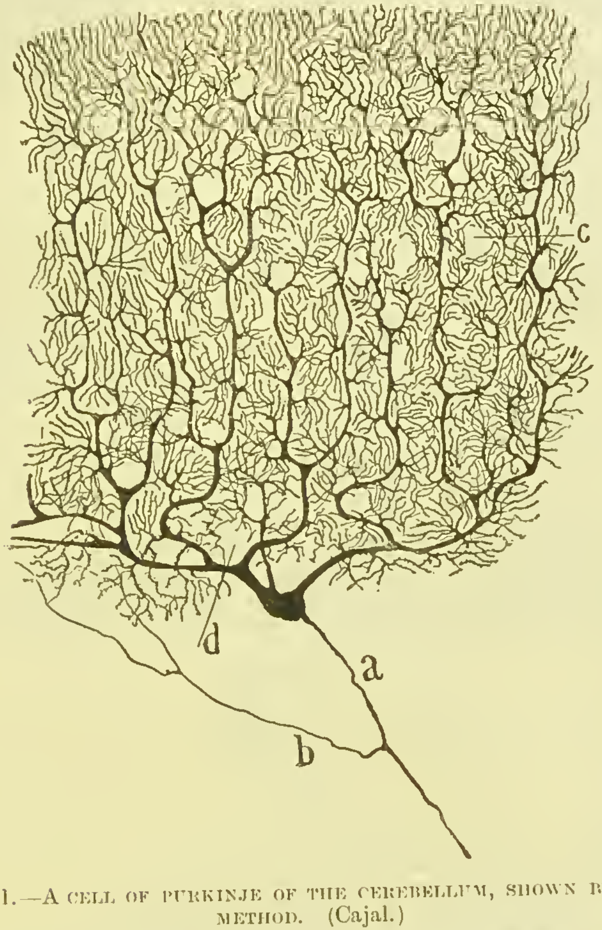
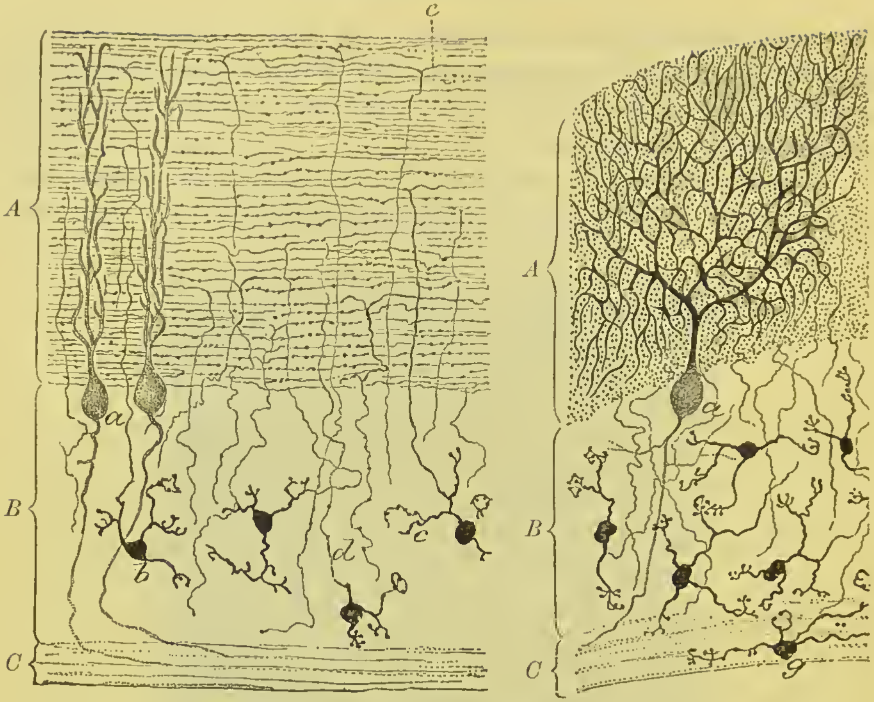


FIG. 561.—A CELL OF PURKINJE OF THE CEREBELLUM, SHOWN BY GOLGI'S METHOD. (Cajal.)
a, axon; *b*, collateral from axon; *c*, *d*, arborisation of dendrons.



FIGS. 562 AND 563.—SECTIONS OF CORTEX CEREBELLI STAINED BY GOLGI'S METHOD. (Cajal.)

FIG. 562.—Section made in the direction of the lamina. FIG. 563.—Section taken across the lamina.

A, outer or molecular layer; *B*, inner or granule layer; *C*, medullary centre.

a, corpuscles of Purkinje; *b*, small granules of inner layer; *c*, a protoplasmic process (dendron) of a granule; *d*, nerve-fibre process of a granule passing into the molecular layer, where it bifurcates and becomes a longitudinal fibre (in fig. 563 these longitudinal fibres are cut across and appear as dots); *e*, bifurcation of another fibre; *g*, a granule lying in the white centre.

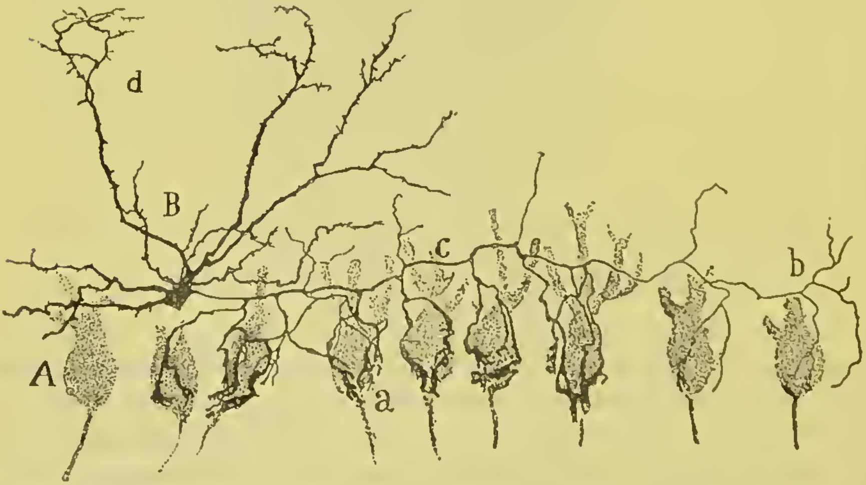


FIG. 564.—BASKET-CELL OF CEREBELLUM SHOWING THE ARBORISATIONS OF ITS AXON OVER THE CELLS OF PURKINJE. (Cajal.)

A, row of Purkinje cells; B, basket-cell of molecular layer; *d*, its dendrons; *c*, its axon; *a* and *b*, endings of axon.

Some of the cells of the granule layer are far larger than the others, and send their much-branching axons amongst the smaller granules (*cells of Golgi*, fig. 566, G). Besides these, other large "granules" have been noticed by Cajal, occurring both in the granule layer and in the white centre, with long axons passing into the white matter of the cerebellum. These are, however, only rarely met with.

Ramifying amongst the cells of the granule layer are peculiar fibres derived from the white centre, and characterised by having pencils of fine short branches at intervals like tufts of moss (fig. 566, *m.f.*). These have been termed by Cajal the *moss-fibres*; they end partly in the granule layer, partly in the molecular layer.

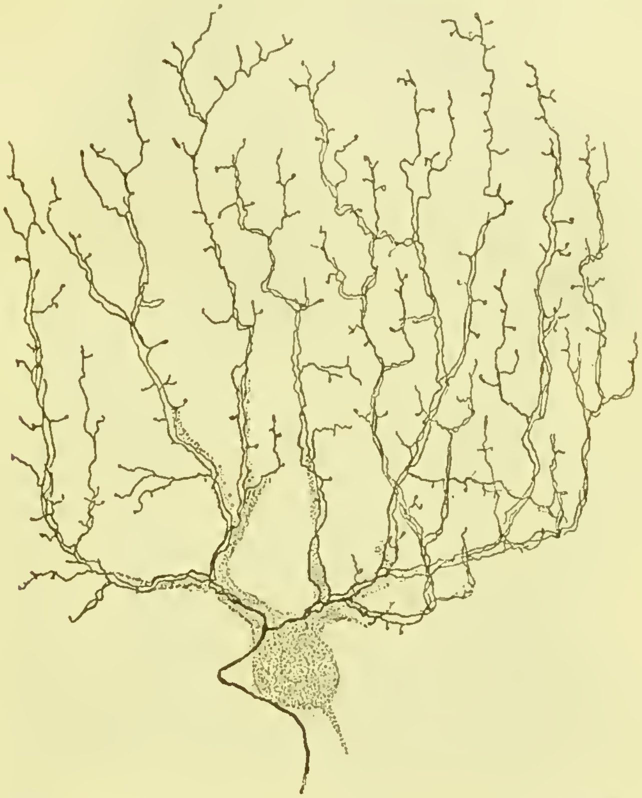


FIG. 565.—ENDING OF A "TENDRIL" FIBRE OVER THE DENDRONS OF A PURKINJE CELL; HUMAN. (Cajal.)

The **neuroglia** of the cerebellum is peculiar in containing, besides the ordinary branched and unbranched neuroglia-cells (fig. 565, *gl*¹, *gl*²), cells which possess long parallel processes which extend through the molecular layer to be attached to the surface of the lamellæ (*gl*³). The cell-bodies of these lie at about the same level as those of Purkinje's cells.

The **peduncles of the cerebellum** have been already studied in connection with the medulla oblongata, pons, and mid-brain. The *inferior peduncle* (restiform body) is composed of ascending fibres derived from the dorsal spino-cerebellar tract, from both olivary nuclei—but chiefly from that of the opposite side; perhaps also from the nuclei of the gracile and cuneate funiculi, from cells and nuclei of the reticular formation of the medulla oblongata, and from the sensory nuclei of the cranial nerves, especially of the vestibular nerve. The fibres of the

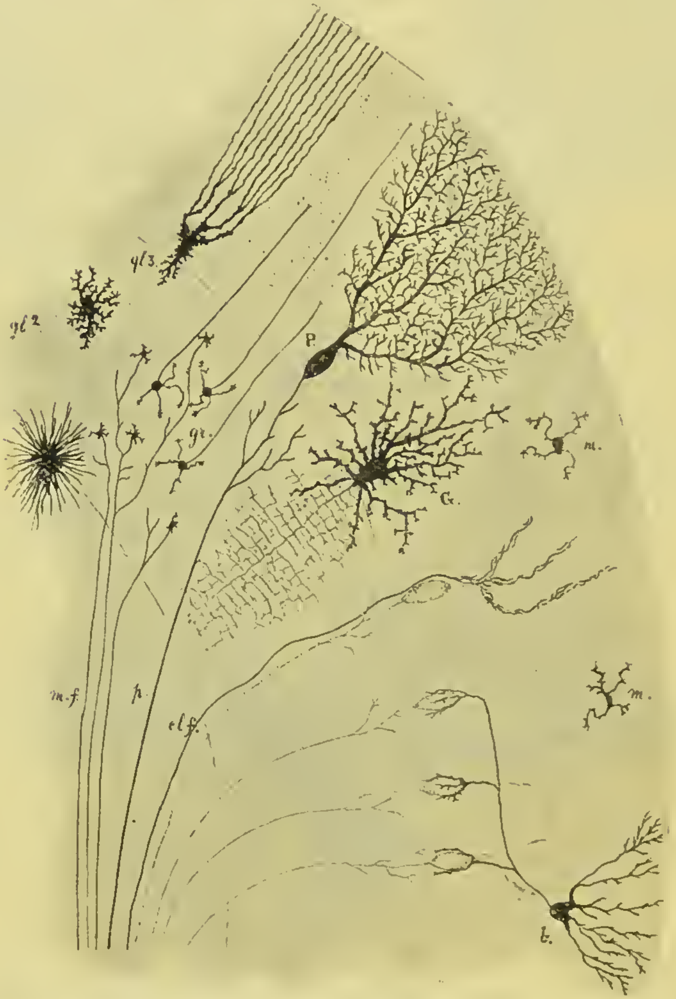


FIG. 566.—DIAGRAMMATIC SECTION OF CEREBELLUM TO SHOW THE CHARACTERS AND RELATIONS OF THE CELLS AND FIBRES MET WITH IN THE SEVERAL LAYERS AS EXHIBITED BY THE CHROMATE OF SILVER METHOD. (After Kölliker.)

P, a cell of Purkinje; *G*, a cell of Golgi; *b*, a basket-cell; *m*, *m*, other cells of the molecular layers; *gr*, granules; *p*, a nerve-fibre of the white substance derived from a Purkinje cell; *m.f.*, "moss"-fibres; *cl.f.*, a climbing fibre; gl^1, gl^2, gl^3, types of neuroglia-cells.

spino-cerebellar tract occupy the outer part of the peduncle. Most of the fibres of the inferior peduncle pass to the vermis, crossing to the opposite side over the fourth ventricle, but before doing so they give off strong collaterals to the hemisphere of the same side. The inferior peduncle also contains a small bundle of fibres descending from the nucleus tecti of the opposite side to the medulla oblongata (Risien Russell) which bends round the superior peduncle to join the inferior peduncle, its fibres lying between those of the superior peduncle and Gowers' bundle. The inferior peduncle contains a very small nucleus of grey matter (Déjerine) which is almost completely concealed amongst the mass of white fibres (fig. 536).

The *middle peduncle* is formed of fibres from the cells of the nuclei pontis which are passing to the opposite hemisphere of the cerebellum.

The *superior peduncle* is formed of fibres which mostly take origin in the corpus dentatum cerebelli, but some are said to arise in the hemisphere and pass through this. The superior peduncles decussate in the mid-brain across the raphe, and their fibres then bifurcate into ascending and descending branches. The ascending branches pass forwards and end in the red nucleus, but some fibres go past this into the ventral part of the thalamus. The descending branches are traceable into the dorsal part of the reticular formation of the pons.

The superior peduncle, as it issues from the hemisphere, is joined by the bundle of Gowers, which runs over it, and passes backwards along its mesial border to the vermis.

STRUCTURE OF THE CEREBRUM.

The grey matter of the **cerebral cortex** is described as if composed of a number of layers, but they are not sharply marked off from one another and they vary in relative development in different regions of the cortex. The cells are for the most part of a pyramidal shape (fig. 567). The following layers are generally distinguishable, but in some parts of the cortex a larger number can be made out:

1. A peripheral stratum (*molecular* or *plexiform layer*, figs. 567, 568, 1) containing scattered nerve-cells and many neuroglia-cells. In the most superficial part of this layer, immediately under the pia-mater, is a thin stratum of medullated nerve-fibres, and besides these the layer contains a large number of fibres, many of which are ramified. They are mostly derived from the deeper nerve-cells of the cortex. Intermingled with these fibres are a certain number of ramified nerve-cells, which have several long horizontally disposed dendrons and a long axon, all of which terminate by arborisation within the

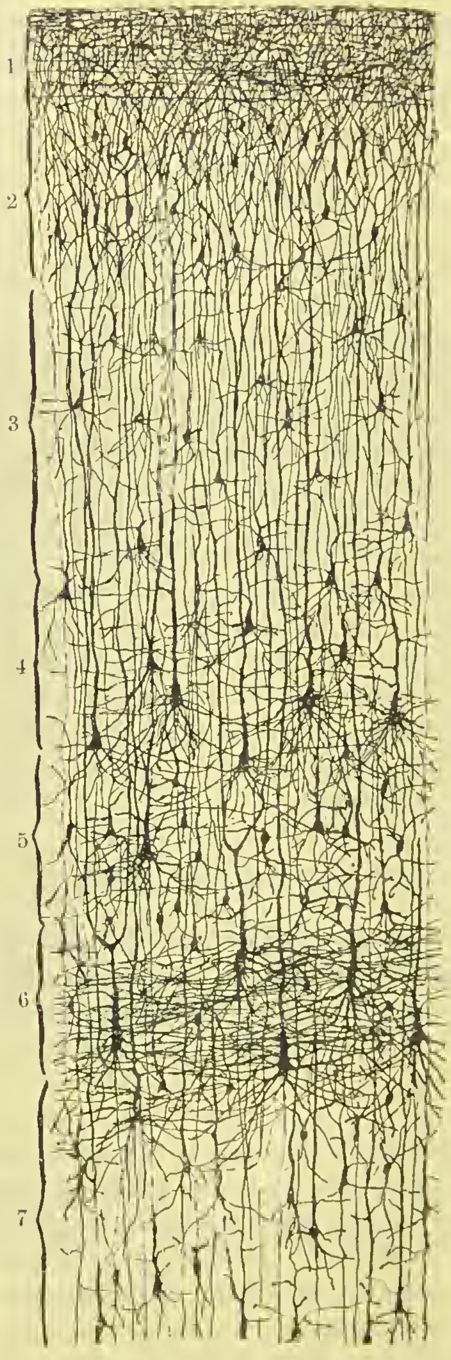


FIG. 567.—ASCENDING PARIETAL (POST-CENTRAL) CONVOLUTION, GOLGI METHOD. (Cajal.)

1, plexiform layer ; 2, small pyramids ; 3, medium pyramids ; 4, superficial large pyramids ; 5, granules ; 6, deep large pyramids ; 7, deep medium pyramids.

superficial layer (*horizontal cells of Cajal*) (fig. 568). Besides these, others of a somewhat similar character but with short axis-cylinder processes occur in this layer.

2. A layer of closely set small pyramidal nerve-cells, several deep (*layer of small pyramids*, fig. 567, 2). This layer also contains other cells with short axons (fig. 578, E, F, G).

3. A layer of medium-sized pyramidal cells less closely set, with small granule-like cells amongst them (*layer of medium-sized pyramids*, fig. 567, 3; fig. 578, J, H, K).

4. A layer of larger pyramidal cells (*superficial large pyramids*, fig. 567, 4).

5. A layer of small irregular cells (*small stellate cells*, fig. 567, 5). The large pyramids may extend down into this layer.

6. A layer of still larger pyramids (*deep large pyramids*, fig. 567, 6). In the motor region of the cortex, which in man is confined to the precentral gyrus and paracentral lobule, pyramidal cells of very large size (giant cells) occur, and are disposed in small clusters or "nests" (Betz, Bevan Lewis). The fibres of the pyramid-tract arise from these giant cells. In some parts of the cortex this layer is absent or is blended with the next layer.

7. A layer of medium-sized pyramidal cells (*deep medium pyramids*, fig. 567, 7).

8. A layer of small scattered cells, many of a fusiform shape (*polymorphous layer*). This layer lies next to the white centre. In the island of Reil it is considerably developed, and is separated from the rest of the grey matter by a layer of white substance. It is here known as the *claustrum*, and on that account the layer is sometimes termed the *claustral layer*.

Some authorities describe the cortex as consisting only of three layers, viz.: the molecular layer, the layer of pyramids, and the layer of polymorphous cells; others of four, five, etc., up to nine. As a matter of fact, the complexity and the number of distinct layers vary in different regions. The pyramidal cells of the cortex are so termed from the shape of the cell-body, which usually gives off several dendrons from the base of the pyramid and one large dendron from its apex. This process extends to the plexiform layer, on approaching which it breaks up into numerous ramifications which have a general vertical direction and extend almost to the outer surface. This apical dendron is beset, both in its undivided part and in its branches, by minute spinous projections (as seen in specimens prepared by the Golgi method). These projections are believed by some authors to be retractile (amœboid) and to be the means of effecting (or breaking) nervous connection with afferent fibres; since they are in some preparations prominent, in others hardly visible; sometimes the dendrons are entirely free from them, and have an even outline or may be slightly moniliform. All the pyramidal cells have a single axon, which is usually directed towards the medullary centre, of which it forms one of the fibres; but the axon sometimes curves back and passes outwards again, ending in arborisations in one of the other layers.

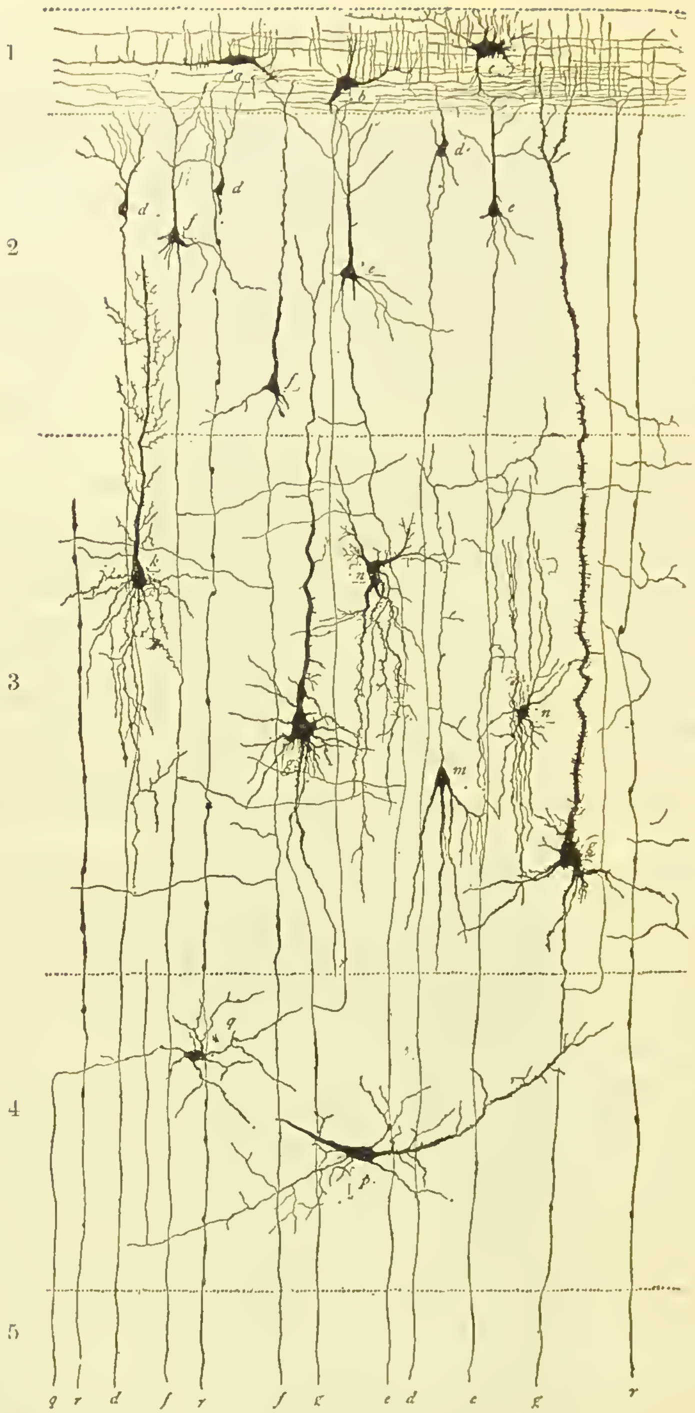


FIG. 568.—DIAGRAM SHOWING THE RELATIONS OF SOME OF THE CELLS IN THE CEREBRAL CORTEX. (Barker, after Starr, Strong, and Leaming.)

1, plexiform layer with cells of Cajal; 2, small (*d*, *e*) and middle sized (*f*) pyramids; 3, large pyramids (*g*, *g*, *k*); also *m*, cell with axon passing towards the surface, but soon ramifying; *n*, *n*, cell of Golgi's second type, with axon ramifying in the adjacent grey matter: one of these belongs to the kind termed by Cajal "double-brush" cells; 4, polymorphous cells, of which *p* sends its axon towards the surface and *q* its axon into the medullary centre, 5, which contains also the axons of the pyramids; *r*, *r*, afferent fibres, ending in the cortex

Intermingled with the pyramids and polymorphous cells are two other kinds of cells, viz.: (1) cells with axis-cylinder process ramifying near the cell-body; these occur in all the layers (fig. 578) and (2) small cells sending their axons towards the plexiform layer (Martinotti), these are found chiefly in the deeper layers of the cortex.

From the white centre bundles of medullated nerve-fibres pass in vertical streaks through the deeper layers of the grey matter to lose themselves amongst the pyramidal cells of the more superficial layers (figs. 574, 577). Many large fibres, however, are seen running not vertically but obliquely into the grey centre from the white matter. Most of the vertically disposed fibres are the nerve-fibre processes of the pyramidal and polymorphous cells, and therefore take origin in the cortex; others, including the oblique fibres just mentioned, are passing into the cortex, probably from the thalamus, to end amongst the cells of the several layers in free arborisations (fig. 570).

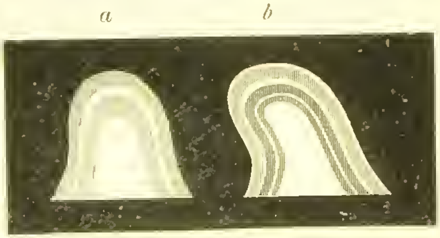


Fig. 569.—Sections of cerebral convolutions. (After Baillarger.) (Natural size.)

a, from the neighbourhood of the calcarine fissure with only one white line clearly visible (the line of Gennari); *b*, ordinary type, with the superficial white layer and outer and inner lines of Baillarger shown.

Besides these vertical strands of fibres there are others which lie in planes parallel to the surface of the cortex, and which are derived partly from the fibres which enter the cortex from the white matter, partly from the collaterals which are given off from the axis-cylinder processes of the cortical cells themselves. The planes in which these fibres occur are (1) near the surface, in the plexiform (molecular) layer: this superficial stratum of white fibres is best marked in the hippocampal region; (2) in the layer of medium-sized pyramids: here the fibres give the appearance of a whitish line in the section of the grey matter (*outer line of Baillarger*, fig. 569, *b*). There is a particularly dense plexus of fibres in this situation in certain regions of the cortex, especially in the occipital lobe (in man in the convolutions bounding the calcarine fissure), producing a very distinct line, here known as the *line of Gennari* (fig. 569, *a*). This plexus of nerve-fibres is in intimate association with certain large and small stellate cells which are characteristic of the visual region. (3) In most regions of the brain, in the plane of the layer of large pyramids, another white line is seen; this is known as the *inner line of Baillarger*. The planes in which these white lines are found are characterised especially in the occipital and temporal lobes, by the presence amongst the pyramids of great numbers of small nerve-cells, amongst which the white fibres of the layers ramify and probably terminate.

The axis-cylinder processes of the pyramidal cells pass into the white centre. Here some of them are continued into the corpus callosum, and through this to the cortex of the opposite hemisphere (*commissural fibres*); others form *association-fibres* which eventually pass again into the grey matter of other parts of the same hemisphere; whilst others again, especially those of the largest pyramidal cells, extend downwards through the corona radiata and internal capsule. These include the *projection-fibres* of the pyramid tract and of the cortico-pontine tract. As the projection fibres pass through the grey and white matter of the hemisphere they give off collateral fibres to the adjacent grey matter, to the corpus callosum, and to the corpus

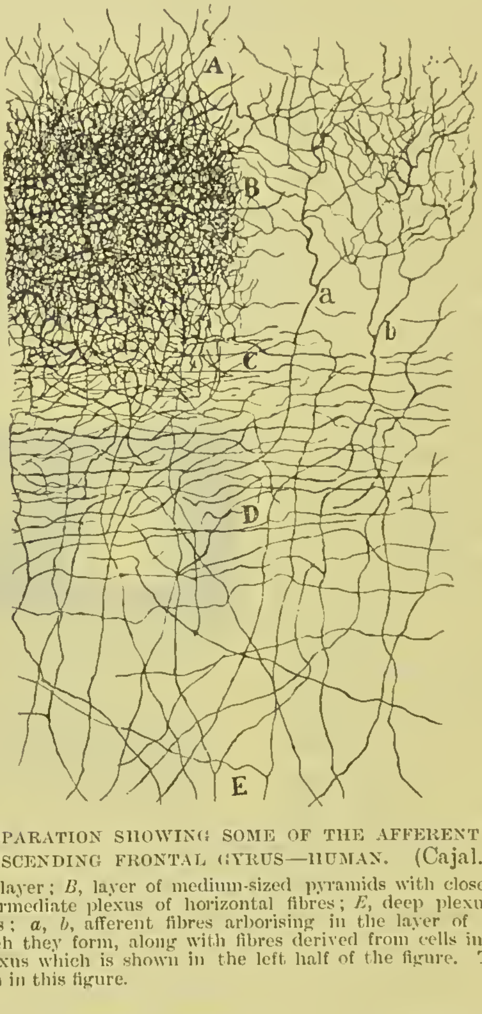


FIG. 570.—PREPARATION SHOWING SOME OF THE AFFERENT FIBRES OF THE ASCENDING FRONTAL GYRUS—HUMAN. (Cajal.)

A, part of second layer; *B*, layer of medium-sized pyramids with close terminal plexus; *C* to *D*, intermediate plexus of horizontal fibres; *E*, deep plexus of large oblique afferent fibres; *a*, *b*, afferent fibres arborising in the layer of middle pyramids, amongst which they form, along with fibres derived from cells in the cortex itself, the dense plexus which is shown in the left half of the figure. The efferent fibres are not shown in this figure.

striatum and optic thalamus, and some probably end in these masses of grey matter. According to Cajal, in the brain of man as compared with the lower mammals, there is a marked preponderance of the cells with short axis-cylinder ramifying near the cell-body. Such cells are most numerous in the layer of stellate cells and in the layer of small pyramids.

The neuroglia of the cortex cerebri contains all three types of glia-cell (p. 181), viz.: spider cells, arborescent cells, and cells the body of which is placed near the surface while the processes extend for a considerable distance vertically into the grey matter (fig. 571). The ependyma cells of the ventricles are also prolonged, like the cells of the central canal of the cord, in the form of long neuroglia-like fibres into the adjacent grey matter.

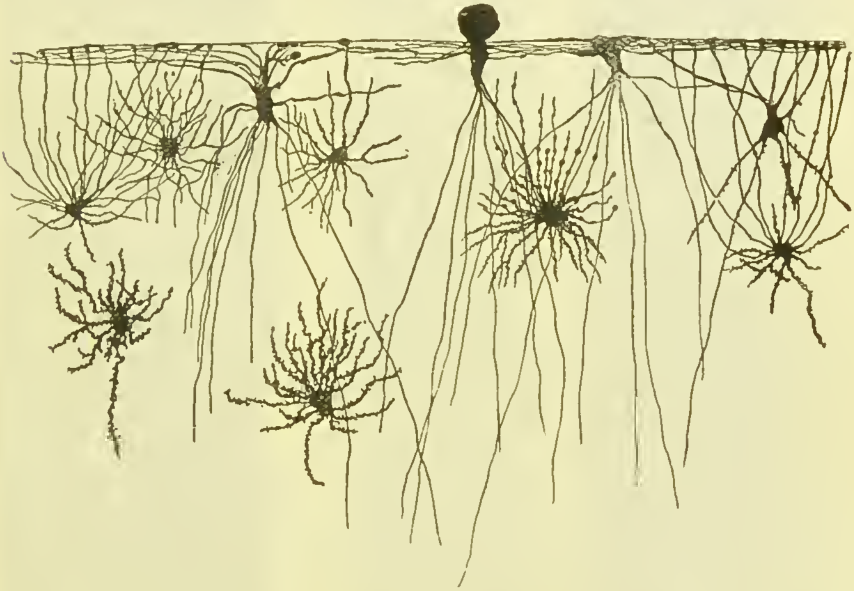


Fig. 571.—Neuroglia cells of cortex cerebri: Golgi method. (G. Retzius.)

Special features of certain parts of the cortex.—There is, as already stated, a great amount of variation met with in the relative extent of development of the above layers. This is exemplified in the accompanying drawings by Cajal (figs. 572 to 577) of certain convolutions in the human brain. From these it will be seen that smaller-sized cells prevail in some regions of the cortex (occipital, temporal); larger and fewer cells in others (frontal, parietal, limbic). Nests or groups of very large "giant" cells are characteristic of the "motor" region (precentral gyrus and paracentral lobule in man and anthropoid

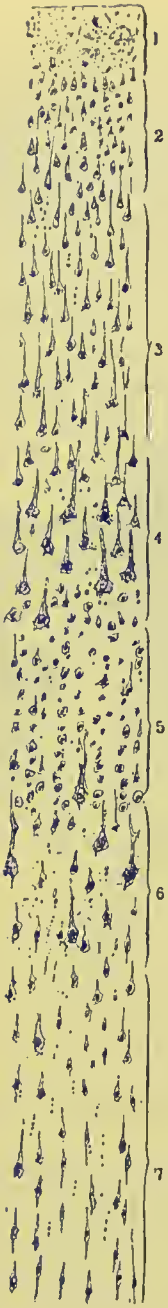


FIG. 572.

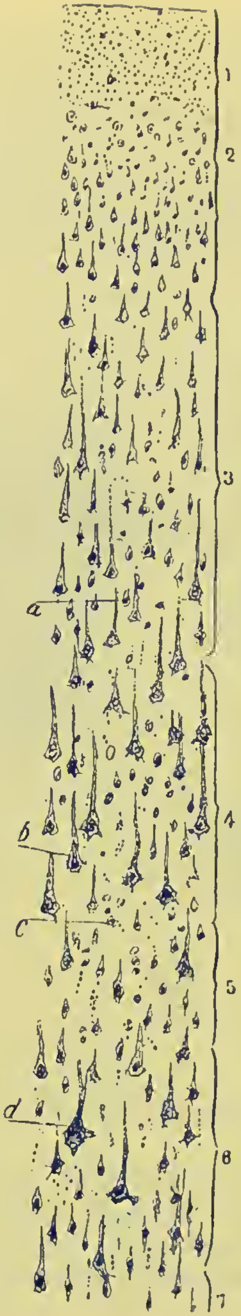


FIG. 573.

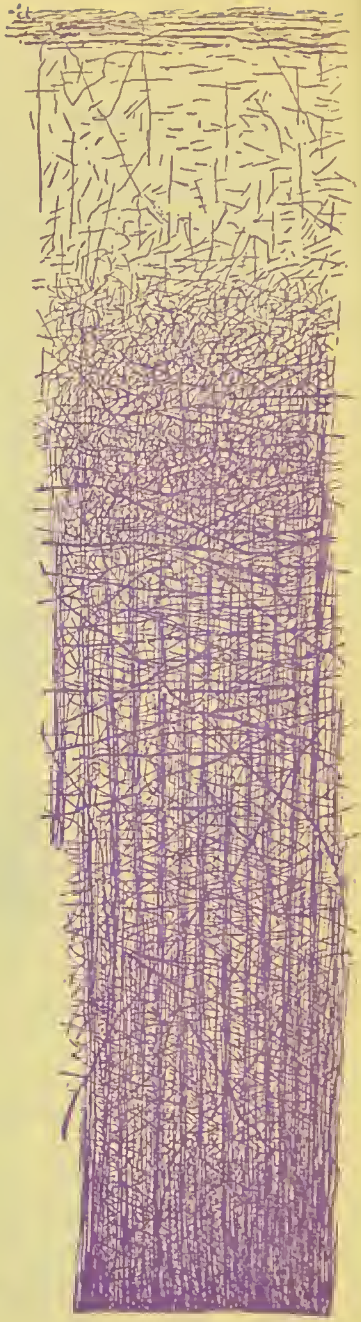


FIG. 574.

FIG. 572.—SECTION OF POST-CENTRAL GYRUS OF MAN, STAINED BY NISSL'S METHOD. (Cajal.)

1, plexiform layer; 2, small pyramids; 3, medium pyramids; 4, superficial large pyramids; 5, small stellate cells (granules); 6, deep large and medium pyramids; 7, fusiform cells.

FIG. 573.—SECTION OF PRECENTRAL GYRUS (MOTOR CORTEX), STAINED BY NISSL'S METHOD. (Cajal.)

1 to 6 as before; *a*, *c*, small cells amongst the pyramids; *b*, a large pyramid; *d*, a giant cell of Betz.

FIG. 574.—SECTION OF ONE OF THE MOTOR CONVOLUTIONS (MAN), STAINED BY WEIGERT-PAL METHOD. (Cajal.)

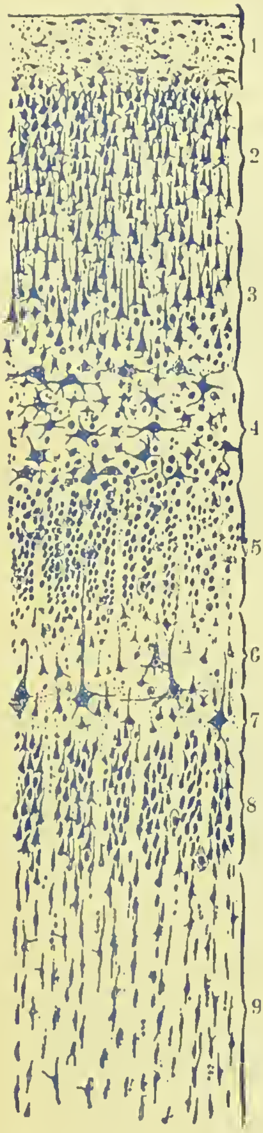


FIG. 575.

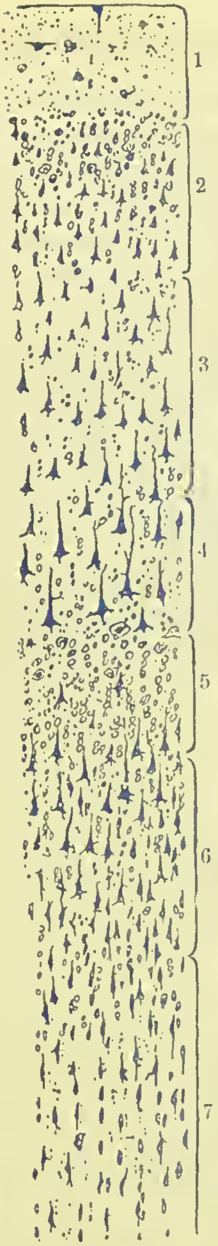


FIG. 576.

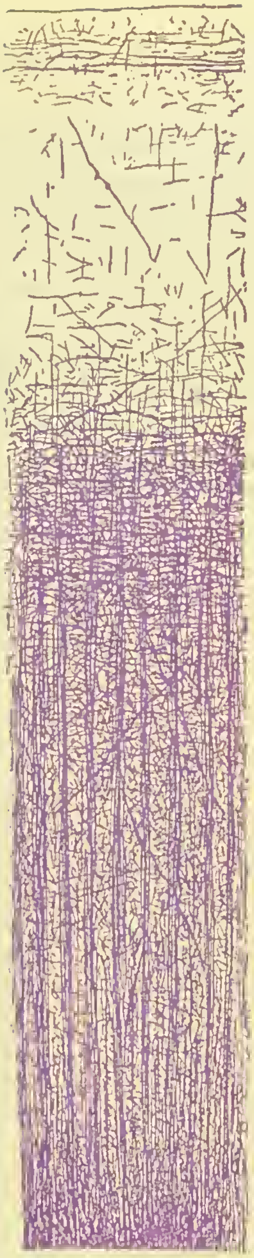


FIG. 577.

FIG. 575.—CALCARINE (VISUAL) CORTEX OF MAN. (Cajal.) Nissl's method.

1, plexiform layer; 2, small pyramids; 3, medium pyramids; 4, large stellate cells (characteristic of this part of the cortex); 5, small stellate cells; 6, a deep plexiform layer, containing some small pyramids; 7, large pyramids; 8, layer of small and medium pyramids with bent ascending axons; 9, fusiform cells.

FIG. 576.—SECTION OF FIRST TEMPORAL GYRUS (ACOUSTIC CORTEX) OF MAN, STAINED BY NISSL'S METHOD. (Cajal.)

1, plexiform layer; 2, layer of small pyramids; 3, superficial medium pyramids; 4, large pyramids; 5, small stellate cells (granules); 6, deep medium pyramids: 7, fusiform cells.

FIG. 577.—SECTION OF THE FIRST TEMPORAL GYRUS (MAN), STAINED BY WEIGERT-PAL METHOD. (Cajal.)

apes); these cells give origin to the fibres of the pyramid tract, and undergo Nissl degeneration when these fibres are severed. The occipital region (in man, the neighbourhood of the calcarine fissure) is especially characterised by the great numbers of small stellate cells and by the presence in the layer superficial to them of a stratum of very large stellate cells with long spreading dendrons (fig. 575, 4): amongst these stellate cells (small and large) the optic fibres from the lateral geniculate bodies ramify. A preponderance of small stellate cells is also seen, but to a less extent, in sections of the temporal lobe; to a still less extent in the prefrontal and parietal regions. The first temporal gyrus is characterised by the presence in nearly all the layers, but especially the deepest, of special large cells with widely spreading dendrons and an axon passing towards the white substance but giving off many collaterals in the grey matter. There are also very many cells with axis-cylinder ramifying in a most

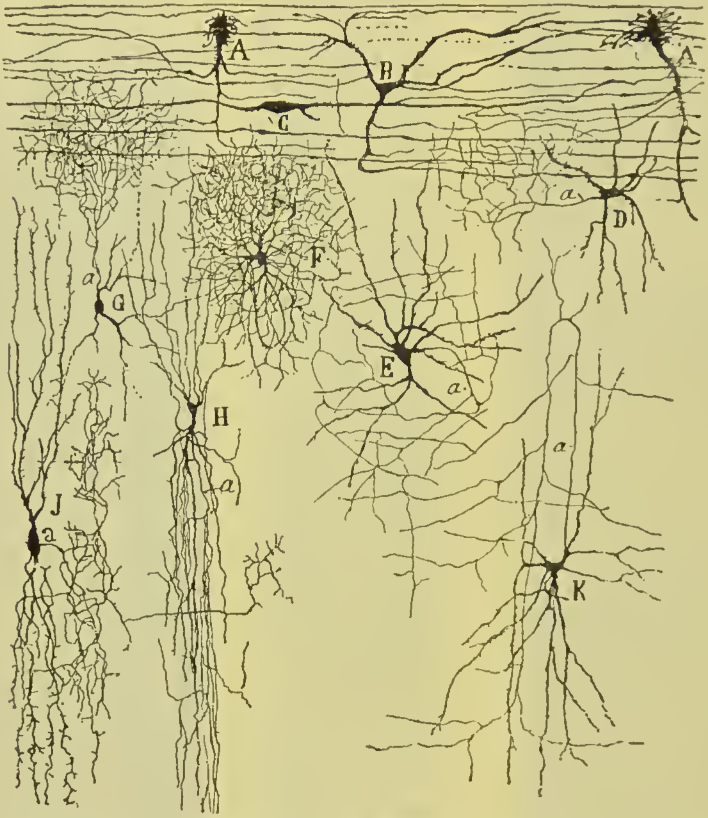


FIG. 578.—SUPERFICIAL LAYERS OF MOTOR CORTEX OF CHILD: GOLGI METHOD. (Cajal.)

A, B, C, cells of Cajal in plexiform layer; D to K, cells of type ii. of Golgi (with axons ramifying near cell-body); H, J, "double-brush" types of cell.

complex manner near the cell-body, mainly in a plane vertical to the surface. The hippocampal gyrus has groups or islets of stellate cells (islets of small cells alternating with islets of larger) in the plexiform layer (see p. 494). The cortex of the insula has special cells similar to those in the first temporal gyrus, and is further characterised by the peculiar spindle-shape of many of the large pyramids.

The size and number of the medullated fibres vary in different regions. In some they are large and numerous (motor part of frontal lobe, calcarine area, hippocampal area), in others fine and much less conspicuous (gyrus fornicatus, temporal area, parietal area, prefrontal area, insula and lobus pyriformis), whilst an intermediate condition presents itself in the occipital area (except the calcarine region), the transverse temporal gyri and superior temporal gyrus, and the part of the frontal immediately in front of the motor region. These differences have been employed by Campbell in attempting to differentiate the functions of the various cerebral regions by a comparison of their structure.[1]

THE RHINENCEPHALON.

The **rhinencephalon** (olfactory region of the telencephalon), on account of the peculiarities of its structure, its importance in most animals, and the fact that it has been the part of the telencephalon to appear first in phylogenetic development merits a special description, although in man and primates generally, and in some other (microsmatic) mammals, it is reduced to a comparatively rudimentary condition. On the other hand, in the so-called osmatic (macrosmatic) mammals there is a hollow olfactory bulb forming the anterior termination of a thick olfactory lobe which broadens out behind, where it is continuous with the hippocampal gyrus and hippocampus. The whole forms a pyriform mass, which is separated from the rest of the cortex by a well-marked fissure—the *limbic fissure*—and has special connections through the anterior commissure and fornix with other parts of the brain on the same and on the opposite side.

In man the rhinencephalon consists anteriorly of the small *olfactory bulb* from which the thin *olfactory tract* extends backwards to the grey matter at the base of the brain and to the hippocampal region. Posteriorly the cortex of the rhinencephalon is doubled in so as to form a projection, the *hippocampus major*, into the descending cornu of the lateral ventricle: its edge here thins off and is continued merely as an epithelial covering to the choroid plexus of the pia-mater, which is invaginated into the ventricle. At this thin edge the white matter comes to the surface as the *fimbria* (which is continuous with the fornix); lying along this is the small and half-concealed *dentate gyrus*, which is formed by the sharp bending of the grey matter, and which is traceable round into the hippocampus major (from this it is separated by the hippocampal fissure), while this again is directly continuous externally with the *gyrus hippocampi.* The olfactory lobe (tract) is connected directly with the hippocampal region by its lateral root, whilst a mesial root passes into the anterior commissure and connects it with the rhinencephalon of the opposite side. The structure and

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[1] For further details regarding the different regions of the cortex and illustrations of their structure the student is referred to Schäfer and Symington's *Neurology* (Longmans, London, 1908).

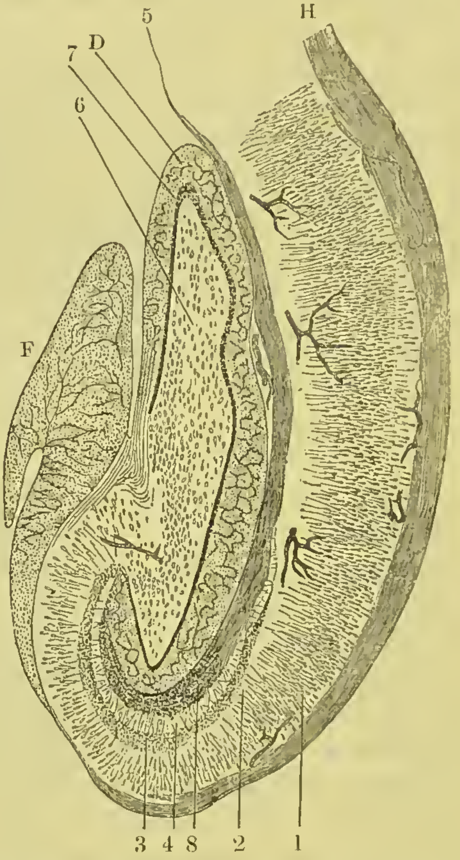

FIG. 579.—SECTION ACROSS THE HIPPOCAMPUS MAJOR, DENTATE FISSURE, DENTATE FASCIA AND FIMBRIA. (W. Krause.)

D, fascia dentata, or dentate convolution; F, fimbria, composed of longitudinal fibres here cut across; H, medullary centre of the hippocampal gyrus prolonged around the hippocampus, as the so-called alveus, into the fimbria; 1, layer of large pyramidal cells; 2, their processes (stratum radiatum); 3, stratum granulosum; 4, plexiform layer (stratum laciniosum); 5, superficial white layer; 6, nerve-cells of fascia dentata: 7, stratum granulosum of fascia dentata; 8, termination of superficial white layer, its fibres becoming longitudinal.

connections of all these parts as they occur in man may be briefly alluded to.

In the region of the hippocampus major (figs. 579, 580), the cortex is simpler in structure than elsewhere, and in the hippocampus major

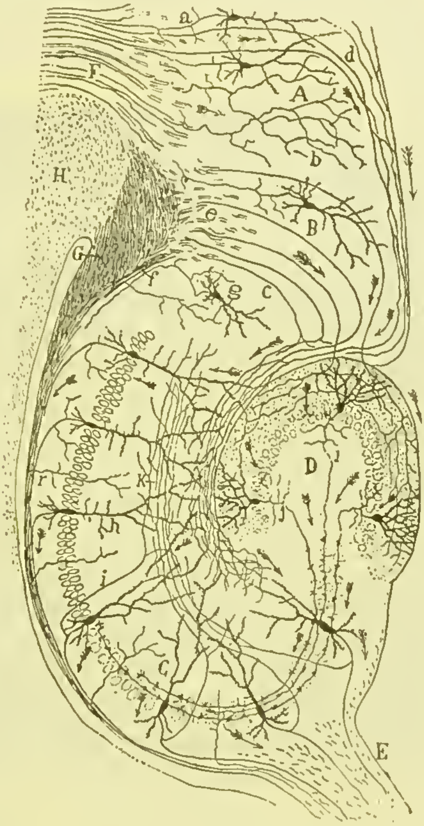

FIG. 580.—HIPPOCAMPAL REGION: GOLGI METHOD. (Cajal.)

A, B, hippocampal gyrus; C, hippocampus major; D, dentate gyrus; E, fimbria; F, white matter of hippocampal gyrus; G, in lateral ventricle; the line points to the crossed spheno-hippocampal bundle; H, fibres of corpus callosum.

a, efferent fibres of hippocampal gyrus; *b*, afferent fibres of hippocampal gyrus; *c*, afferent fibres of hippocampus and dentate gyrus; *d*, others perforating grey matter of hippocampal gyrus; *e*, others cut obliquely; *f*, fibres of alveus; *g*, *h*, cells of hippocampus major sending their axons into the alveus and towards the fimbria; *i*, *k*, collaterals from these axons passing to the molecular layer; *r*, collateral fibres of alveus. The arrows indicate the probable course of the nerve impulses.

itself, which is an infolded part of the cortex, the pyramids are reduced to a single layer of large cells lying in the deeper portion and sending their apical dendrons as long fibres into the plexiform layer. The plexiform layer and the superficial white stratum which overlies it are both very strongly marked, the plexiform layer having a distinctly reticular aspect, due partly to neuroglia cells, partly to the arborescence of the dendrons of the pyramids: the plexiform layer is here termed *stratum laciniosum*; internal to it near the dentate gyrus is a layer of closely packed small cells termed *stratum granulosum.* The pyramidal cells lie close to the white layer known as the *alveus.* This is the part of the hippocampus seen within the ventricle, and represents the white matter of the hemisphere. The alveus is prolonged externally into the *fimbria*, in which its fibres become longitudinal in direction and are continued into part of the fornix.

In the dentate gyrus (*fascia dentata*, figs. 579, 580, D) the pyramidal cells (6) are arranged in an irregularly radiating manner, occupying the centre of the convolution, and surrounded by a ring of closely packed small cells (*stratum granulosum*, fig. 579, 7). External to these is a thick plexiform layer, occupied by interlacing fibres (*stratum laciniosum*).

The anterior part of the hippocampal gyrus, which is known as the lobus pyriformis, and receives the lateral root of the olfactory tract, is characterised by the presence in the plexiform layer of peculiar nests of nerve-cells. The cells in these nests are of two types, viz., large polymorphous cells and small pyramidal cells, each being confined to its own nest. This part of the cortex is regarded by Cajal as the true olfactory region. In some animals the anterior perforated space forms a distinct prominence of the cortex (tuberculum olfactorium) and this is also characterised by cell-nests (islets of Calleja). They also occur in the cortex of the hippocampal fissure.

The **olfactory tract** is an outgrowth of the brain which was originally hollow, and remains so in many animals; but in man the cavity has become obliterated, and the centre is occupied by neuroglia, containing no nerve-cells. Outside the central neuroglia lies the white or medullary substance, consisting of bundles of longitudinal white fibres. Most externally is a thin superficial layer of neuroglia.

The **olfactory bulb** (fig. 581) has a more complicated structure. Dorsally there is a flattened ring of longitudinal white bundles inclosing neuroglia (1, 2, 3), as in the olfactory tract, but below this ring several layers are recognised as follows:

1. A *white or medullary layer* (fig. 581, 4, 5), characterised by the presence of a large number of small cells ("granules") with reticulating bundles of medullated nerve-fibres running longitudinally between them.

2. A *layer of large nerve-cells* (6), with smaller ones ("granules") intermingled, the whole embedded in an interlacement of fibrils which are mostly derived from the cell-dendrons. From the shape of most of the large cells of this layer (fig. 582, *m.c.*) it has been termed the

"mitral" layer. These cells send their axons upwards into the next layer, and they eventually become fibres of the olfactory tract and pass along this to the base of the brain, giving off numerous collaterals into the bulb as they run backwards.

3. The *layer of olfactory glomeruli* (fig. 581, 7; fig. 582, *gl.*). This consists of rounded nest-like interlacements of fibrils which are derived on the one hand from the terminal arborisations of the non-medullated olfactory fibres which form the subjacent layer, and on the other hand from arborisations of dendrons of the large "mitral" cells of the layer above. There are also a few small nerve-cells immediately external to and extending within the glomeruli (periglomerular cells). These are short axoned cells and appear to connect neighbouring glomeruli.

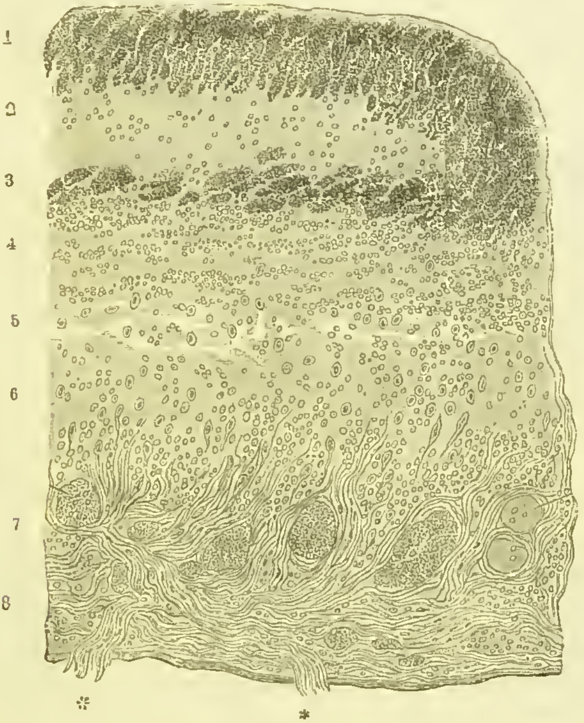

Fig. 581.—Section across a part of the olfactory bulb. (Henle.)

1, 3, bundles of very fine transversely cut nerve-fibres, forming the flattened medullary ring, inclosing the central neuroglia, 2: this ring is the anterior continuation of the olfactory tract; 4, 5, white layer with numerous small cells (granules); 6, mitral-cell layer; 7, layer of olfactory glomeruli; 8, layer of olfactory nerve-fibres, bundles of which are seen at * passing through the cribriform plate of the ethmoid bone.

4. The *layer of olfactory nerve-fibres* (fig. 581, 8; fig. 582, *olf.n.*). These are all non-medullated, and are continued from the olfactory fibres of the olfactory mucous membrane of the nasal fossæ. In this mucous membrane they take origin from the bipolar olfactory

cells, which are characteristic of the membrane (see Lesson XLV. fig. 621), and they end in arborisations within the olfactory glomeruli, where they come in contact with the arborisations of the mitral cells.

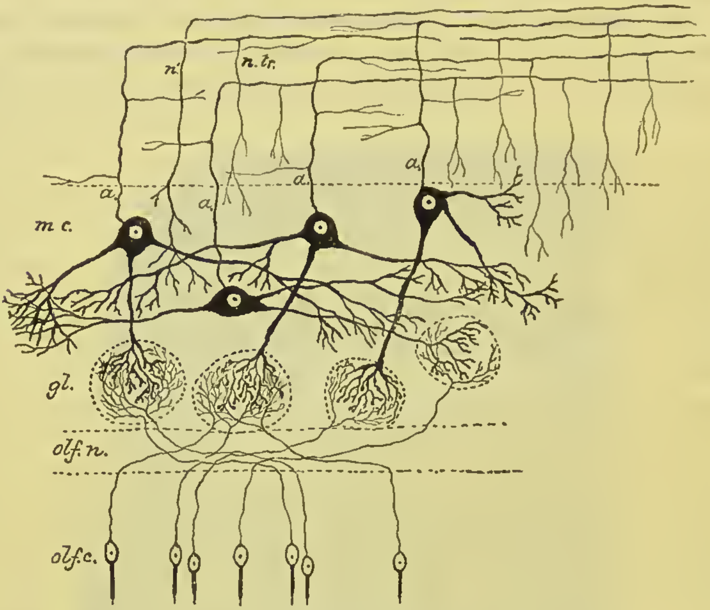

FIG. 582.—DIAGRAM TO SHOW THE RELATIONS OF CELLS AND FIBRES IN THE OLFACTORY BULB.

olf.c., olfactory cells of M. Schultze in the olfactory mucous membrane, sending their basal processes as non-medullated nerve-fibres into the deepest layer of the olfactory bulb (*olf.n.*); *gl.*, olfactory glomeruli containing the terminal arborisations of the olfactory fibres and of processes from the mitral cells; *mc.*, mitral cells, sending processes down to the olfactory glomeruli, others laterally to end in free ramifications in the nerve-cell layer, and their axis-cylinder processes, *a*, *a*, upwards, to turn sharply backwards and become fibres of the olfactory tract (*n.tr.*). Numerous collaterals are seen coming off from these fibres; *n'*, a nerve-fibre of the olfactory tract ending in a free ramification in the olfactory bulb.

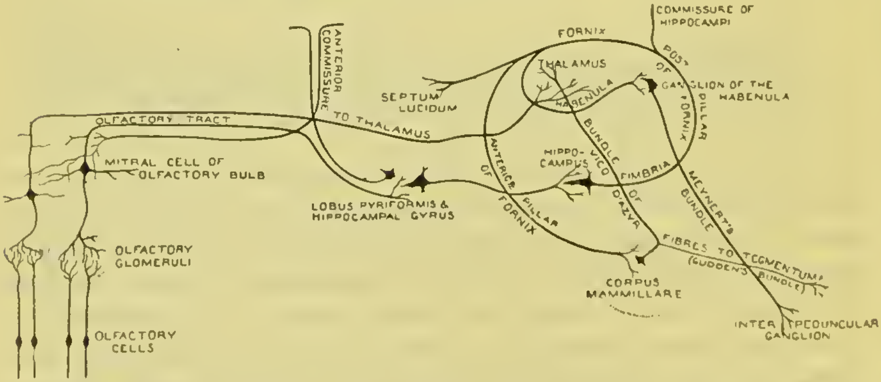

FIG. 583.—DIAGRAM OF THE OLFACTORY PATH IN THE BRAIN. To simplify the diagram the various divarications of the olfactory path have been represented by branchings of individual fibres, although in some cases the divarication is brought about by the turning aside of bundles of entire fibres.

The relations of the olfactory cells and fibres to the mitral cells, and the continuation of the axis-cylinders of the latter upwards and backwards in the olfactory tract, are shown in the accompanying diagrams (figs. 582, 583). Besides these centripetal nerve-fibres there are a certain number of centrifugal fibres which end by ramifying in the olfactory bulb amongst the mitral cells.

As is seen in fig. 583, many of the fibres of the olfactory tract pass to the hippocampal region of the brain, terminating by arborescence in the grey matter (molecular layer) of the base of the olfactory lobe in the region of the anterior perforated space, as well as in that of the uncus and the hippocampal gyrus. Fibres are also given off from the olfactory tract to the *anterior commissure* which proceed to the opposite tract and bulb. Besides these the anterior commissure contains many fibres which are passing from the hippocampal region on one side to the corresponding region on the opposite side of the brain. From the pyramid-cells of the base of the olfactory lobe and hippocampal gyrus fibres pass to the grey matter of the hippocampus, and from the pyramid-cells of the hippocampus others proceed by way of the fimbria and fornix to the hippocampus of the other side, to the subcallosal gyrus and septum pellucidum, to the ganglion of the habenula, and finally by the anterior pillar of the fornix to the corpora mamillaria.

CORPUS STRIATUM.

Besides the grey matter of the cerebral cortex the cerebral hemispheres conceal in their deeper parts certain other masses of grey substance (fig. 584). The principal of these are the *corpus striatum* (*nucleus caudatus*, *n.c.*, and *nucleus lenticularis*, *n.l.*) and *optic thalamus* (*th.*). Between them run the bundles of white fibres which are passing downwards to the crus cerebri, forming a white lamina termed the *internal capsule.* Above the level of these nuclei the internal capsule expands into the medullary centre of the hemisphere. Below the optic thalami are the prominent ganglia known as *corpora albicantia* or *mamillaria.* Of these the optic thalami and corpora mamillaria have already been noticed.

The **nucleus caudatus** of the corpus striatum is composed of a reddish-grey substance containing cells some with long, others with short axis-cylinders; some of the former being very large. It receives fibres from the part of the internal capsule which separates it from the nucleus lenticularis, and next to the lateral ventricle it is covered by a thin layer of neuroglia, and over this by the epithelium of the cavity (ependyma).

The **nucleus lenticularis,** which corresponds in position internally with the island of Reil externally, is divided by two white laminæ into three zones. It is separated from the nucleus caudatus and optic thalamus by the *internal capsule* (fig. 584, *i.c.*), which consists of the bundles of medullary fibres which are passing between the white centre of the hemisphere and the crus cerebri; it receives on its inner side many white fibres from the capsule, and these impart to it a radially striated aspect. Many of the nerve-cells of the nucleus lenticularis contain yellow pigment. The fibres of the *ansa lenticularis* appear to rise from some of them, but the exact course and destination of these fibres is not known.

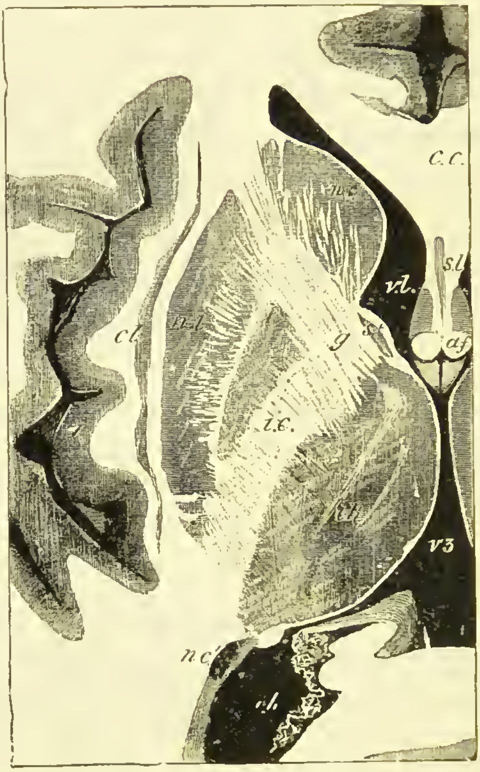

Fig. 584.—Horizontal section through the optic thalamus and corpus striatum. Natural size.

v.l., lateral ventricle, its anterior cornu; *c.c.*, corpus callosum; *s.l.*, septum pellucidum; *a.f.*, anterior pillars of the fornix; *v3*, third ventricle; *th*, thalamus opticus: *st.*, stria medullaris; *nc.*, nucleus caudatus, and *nl.*, nucleus lenticularis of the corpus striatum; *i.c.*, internal capsule; *g*, its angle or genu; *nc'.*, tail of the nucleus caudatus appearing in the descending cornu of the lateral ventricle; *cl.*, claustrum; *I*, island of Reil.

The **internal capsule** (fig. 584), which is continued below into the *crusta* (*pes*) of the crus cerebri, consists mainly of projection-fibres, which are derived from the cortex cerebri, and are passing down to the thalamus, mid-brain, pons, medulla oblongata, and spinal cord. A horizontal section across the internal capsule shows it to be bounded laterally by the lenticular nucleus, mesially by the caudate nucleus, the stria medullaris, and the optic thalamus. Its section shows a sharp bend—the genu. The fibres from the motor region of the cortex (pyramid-tract) pass down in the part of the capsule extending from the genu as far as the posterior limit of the lenticular nucleus. In this area the fibres for the head and eyes are massed chiefly in the anterior part: those of the lower limb in the posterior part, and those of the face, arm, and trunk occupy intermediate positions from before backward, in the order named (Beevor and Horsley), but without being strictly confined to definite zones.

The fibres from the cortex to the thalamus lie mainly in the anterior limb of the capsule, while the afferent fibres from the thalamus to the cortex occur in the posterior part of the posterior limb, but extend forwards so as to mingle with the descending fibres just referred to as belonging to the pyramid-tract.

The **membranes of the brain** are similar in general structure to those of the spinal cord. The dura mater is, however, more closely adherent to the inner surface of the bony enclosure than is the case in the vertebral canal. The arachnoid is in many places close to the dura mater, and separated by a wide subarachnoid space (which is bridged across by finely reticulating bands of areolar tissue) from the pia mater. In the vicinity of the longitudinal sinus, small rounded elevations (arachnoidal villi, Pacchionian glands) project into the dura mater, and even become embedded in the skull itself. The pia mater is closely adherent to the surface of the brain, and dips into all the sulci, but without forming actual folds (Tuke). In it the blood-vessels ramify before passing into the substance of the brain, and they are accompanied, as they thus enter the cerebral substance, by prolongations of the pia mater, which do not, however, closely invest them, but leave a clear space around each vessel, presumably for the passage of lymph (perivascular space). The capillary network is much closer in the grey than in the white matter.

LESSONS XLVI., XLVII., AND XLVIII.

STRUCTURE OF THE EYELIDS AND OF THE PARTS OF THE EYEBALL.

1. Sections of the eyelid vertical to its surfaces and transverse to its long axis.

Notice the long sacculated Meibomian glands lying in dense connective tissue close to the conjunctival surface, their ducts opening at the margin of the lid. External to these the small fibres of the orbicularis palpebrarum are cut across ; a few of the fibres of the muscle lie on the conjunctival side of the duct. A short distance from the Meibomian gland may be observed a tolerably large sebaceous gland ; outside this again are the eyelashes. In the skin covering the outer surface of the eyelid a few small hairs may be seen. At the attached part of the eyelid are some bundles of involuntary muscular fibres cut longitudinally in the section, and in the upper eyelid the fibrous attachment of the elevator muscle may be observed attached to the dense connective tissue.

Make a general sketch under a low power.

2. Sections through the posterior part of an eyeball (man, pig). These sections will show the relative thickness of the several coats and the layers of which each coat is formed. Sections which pass through the point of entrance of the optic nerve will also exhibit the manner in which the nerve-fibres pierce the several coats to reach the inner surface of the retina. The modifications which are found in the neighbourhood of the yellow spot may be made out in sections through that region ; but they must be taken from the human eye, or from that of the ape.

3. Sections of the anterior half of an eyeball. These sections should pass through the middle of the cornea. The lens may be left *in situ*, but this renders the preparation of the sections and the mounting of them difficult on account of the extreme hardness which is imparted to the lens-tissue by alcohol.[1]

In these sections make a general sketch under a low power, showing the relations of the several parts one with another ; and study carefully, and sketch in detail, the layers of the cornea, the junction of the cornea and sclerotic, the ciliary muscle, the muscular tissue of the iris, the mode of suspension of the lens, and the pars ciliaris retinæ.

4. Mount in glycerine thin tangential sections of a cornea stained with chloride of gold by Cohnheim's method ; if from the frog, the cornea can be torn with fine forceps into thin lamellæ, which are mounted whole. Sketch three or four of the connective-tissue cells (corneal corpuscles). The arrangement and distribution of the nerve-fibres and their termination amongst the epithelium-cells as shown in chloride of gold preparations have been already studied (Lesson XIX.).

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[1] The celloidin method of embedding is well adapted for preparations of this kind.

5. Mount in glycerine or dammar sections of a cornea which has been stained with nitrate of silver. Notice the branched cell-spaces corresponding with the connective-tissue cells of the last preparation.

[This preparation is best made by rubbing the surface of the cornea of a recently killed animal with lunar caustic, first scraping off the epithelium with a scalpel. After ten minutes (by which time the nitrate of silver will have penetrated the thickness of the cornea) the eye is washed with distilled water, and exposed to the light. When brown, tangential sections may be made, for which purpose the stained cornea may be hardened in spirit.]

6. Remove the sclerotic from the anterior part of an eye which has been preserved in Müller's fluid, and tear off thin shreds from the surface of the choroid, including amongst them portions of the ciliary muscle. Stain the shreds with hæmatoxylin and mount them in glycerine. Sketch the branched pigment-cells, the elastic network, the mode of attachment of the fibres of the ciliary muscle, etc.

7. Injected preparation of choroid and iris. Mount portions of the choroid coat and iris from an eye (preferably of an albino animal), the blood-vessels of which have been filled with coloured injection. Make sketches showing the arrangement of the capillaries and veins.

8. Teased preparation of human retina. Break up with needles in a drop of glycerine a minute fragment of retina which has been placed in 1 per cent. osmic acid solution for some hours, and has subsequently been kept in dilute glycerine. Complete the separation of the retinal elements by tapping the cover-glass. Draw carefully under a high power some of the isolated elements—*e.g.* the rods and cones with their attached fibres and nuclei, the inner granules, the ganglion-cells, the fibres of Müller, hexagonal pigment-cells, etc. In some of the fragments the arrangement of the elements in the retinal layers may be made out even better than in the actual sections.[1]

Measure the length and diameter of some of the cones, the length of the cone-fibres, and the diameter of some of the outer and inner nuclei.

9. Teased preparation of frog's retina. To be prepared in the same way as 8. Notice the very large rods, their outer segments breaking up into disks, and the relatively small cones. Also the pigment extending between the rods, the distance varying according as the eye has been kept in the dark or in the light. A fresh frog-retina should also be teased in salt solution.

10. Sections of retina of ox or dog, which have been prepared by Golgi's method. A curled-up piece of fresh retina is placed in osmium-bichromate mixture and is subsequently treated with nitrate of silver solution.[2]

11. Teased preparation of lens. Separate in water the fibres of a crystalline lens which has been macerated for some days in bichromate of potassium or dilute formol solution. Sketch some of the fibres, together and separate.

The **eyelids** (fig. 585) are covered externally by the skin, and internally or posteriorly by a mucous membrane, the *conjunctiva*, which is reflected from over the globe of the eye. They are composed in the main of connective tissue, which is dense and fibrous under the conjunctiva, where it forms what is known as the *tarsus*.

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[1] For the distribution of the nerve-fibres and cell-processes within the retina Golgi's silver chromate method should be employed (see § 10).

[2] See Appendix. Cajal's reduced silver method may also be used.

Embedded in the tarsus is a row of long sebaceous glands (the *Meibomian glands, f*), the ducts of which open at the edge of the eyelid. The rest of the thickness of the eyelid is composed of a somewhat loose connective tissue, and contains the bundles of the *orbicularis* muscle (*b*). In the upper eyelid the *levator palpebræ* is inserted into the tarsus by a fibrous expansion, and some bundles of involuntary muscle are also present near the attachment of the eyelid. The skin has the usual structure; it contains small sweat-glands, and the follicles of small hairs, and, in addition, at the edge of the eyelid, the

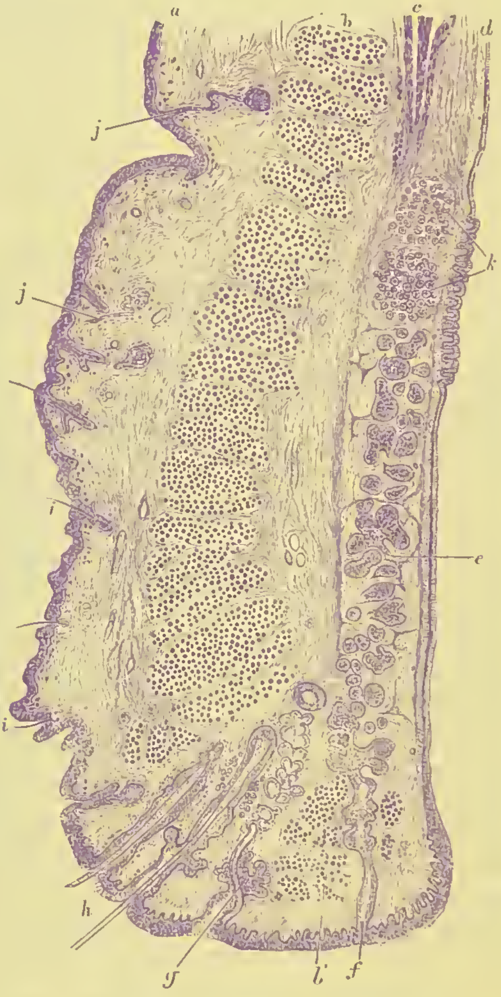


FIG. 585.—VERTICAL SECTION THROUGH THE UPPER EYELID. (Waldeyer.)

a, skin; *b*, orbicularis; *b'*, ciliary bundle; *c*, involuntary muscle of eyelid; *d*, conjunctiva; *e*, tarsus with Meibomian gland; *f*, duct of the gland; *g*, sebaceous gland near eyelashes; *h*, eyelashes; *i*, small hairs in outer skin; *j*, sweat-glands; *k*, posterior tarsal glands.

large hair-follicles from which the eyelashes grow. The epithelium of the conjunctiva palpebræ is columnar, passing at the edge of the lid into the stratified epithelium of the skin; it also becomes stratified in the part which is reflected over the globe of the eye. The nerves of the conjunctiva terminate for the most part in end-bulbs, which in man are spheroidal, and formed chiefly of a small mass of polyhedral cells; but in the calf and most animals they are elliptical.

The **lacrymal glands** may be mentioned in connection with the eyelid. These are compound racemose glands yielding a watery secretion. Their alveoli are lined by columnar cells, which are normally filled with granules, but, after profuse secretion, these disappear, and the cells become shorter and smaller. The ducts, of which there are several, open at the upper fold of the conjunctiva near its outer extremity.

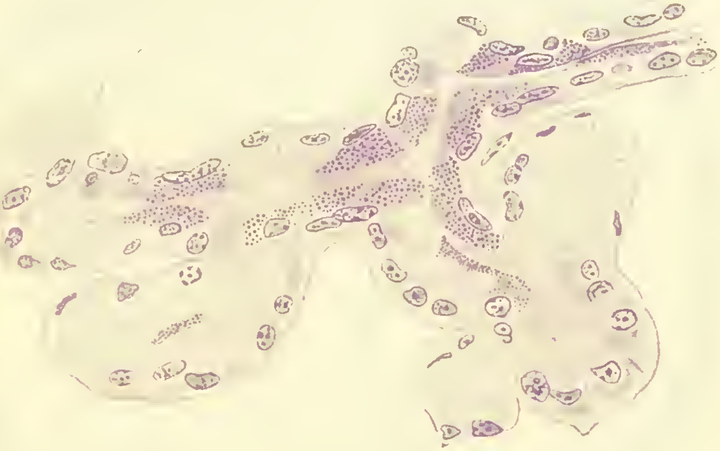


FIG. 586.—ALVEOLI OF LACRYMAL GLAND OF OX. (B. Fleischer.) Magnified 800 diameters.

Some of the cells contain fine darkly stained secretion granules. The larger secretion granules of the ordinary cells of the alveoli are not stained.

THE EYE-BALL.

THE SCLERA AND CORNEA.

The **globe of the eye** (fig. 587) is enclosed by three coats, the cornea-sclera, choroid-iris, and retina. It is filled by the vitreous and aqueous humours and the crystalline lens which lies between them.

The **sclerotic coat** is composed of dense fibrous tissue, the bundles of which are intimately interlaced. It is thickest at the back of the eyeball. It is covered externally with a lymphatic endothelium, while internally it is lined by a layer of connective tissue containing pigment-cells, which give it a brown appearance (*lamina fusca*). At the entrance of the optic nerve the sclerotic is prolonged into the sheath of that nerve, the bundles of which, piercing the coat, give a sieve-like aspect to the part (*lamina cribrosa*).

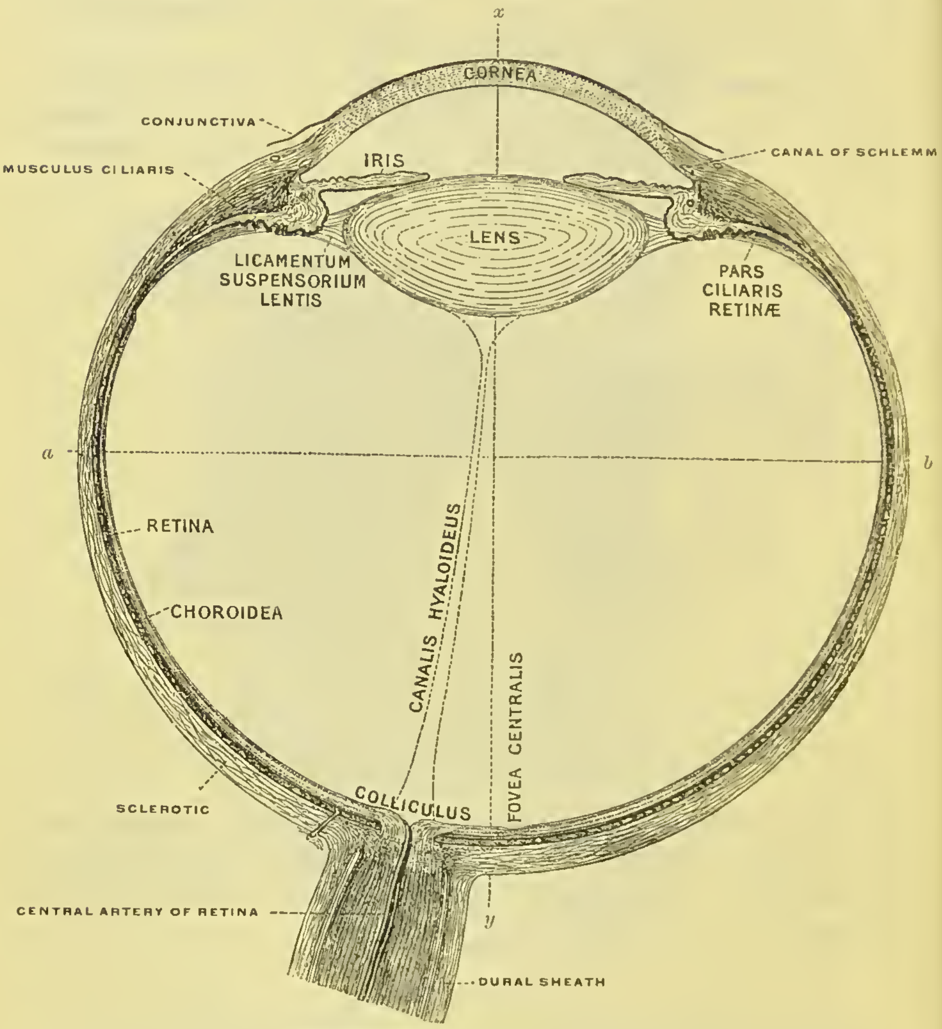


FIG. 587.—DIAGRAM OF A SECTION THROUGH THE (RIGHT) HUMAN EYE PASSING HORIZONTALLY NEARLY THROUGH THE MIDDLE. Magnified about 4 diameters.

a, *b*, equator; *x*, *y*, optic axis.

The cornea (figs. 588, 589) consists of the following layers (enumerated from before back):

1. A *stratified epithelium* continuous with the epithelium of the conjunctiva.

2. A thin lamina of homogeneous connective tissue (*membrane of Bowman*), upon which the deepest cells of the epithelium rest.

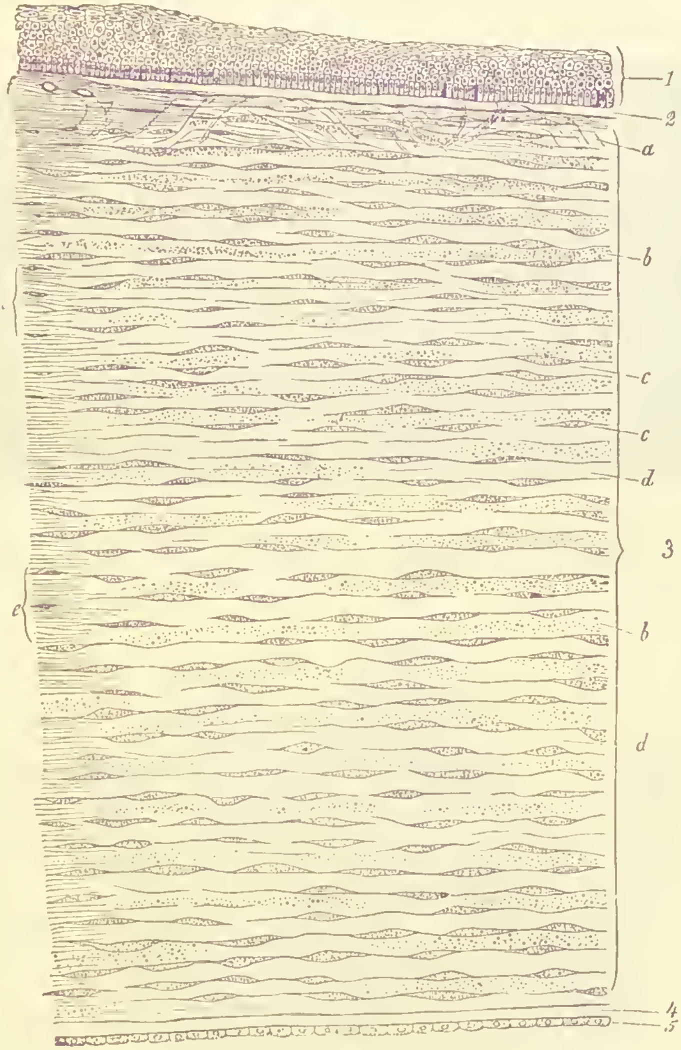


FIG. 588.—VERTICAL SECTION OF HUMAN CORNEA FROM NEAR THE MARGIN. (Waldeyer.) Magnified.

1, epithelium ; *2*, anterior homogeneous lamina ; *3*, substantia propria corneæ ; *4*, posterior homogeneous (elastic) lamina ; *5*, epithelium of the anterior chamber ; *a*, oblique fibres in the anterior layer of the substantia propria ; *b*, lamellæ, with their fibres cut across, producing a dotted appearance ; *c*, corneal corpuscles appearing fusiform in section ; *d*, lamellæ with the fibres cut longitudinally ; *e*, transition to the sclerotic, with more distinct fibrillation, and surmounted by a thicker epithelium ; *f*, small blood-vessels cut across near the margin of the cornea.

3. A thick layer of fibrous connective tissue which forms the *proper substance* of the cornea. This is continuous laterally with the tissue of the sclerotic. It is composed of bundles of white fibres arranged in

regular laminæ, the direction of the fibres crossing one another at right angles in the alternate laminæ. Between the laminæ lie flattened

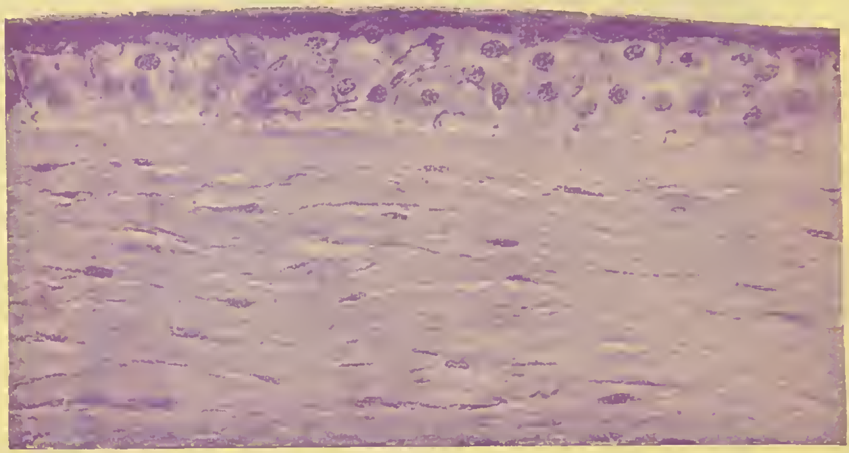


FIG. 589.—SECTION OF HUMAN CORNEA, SHOWING THE STRATIFIED EPITHELIUM, THE MEMBRANE OF BOWMAN, AND THE SUPERFICIAL LAYERS OF THE PROPRIA.

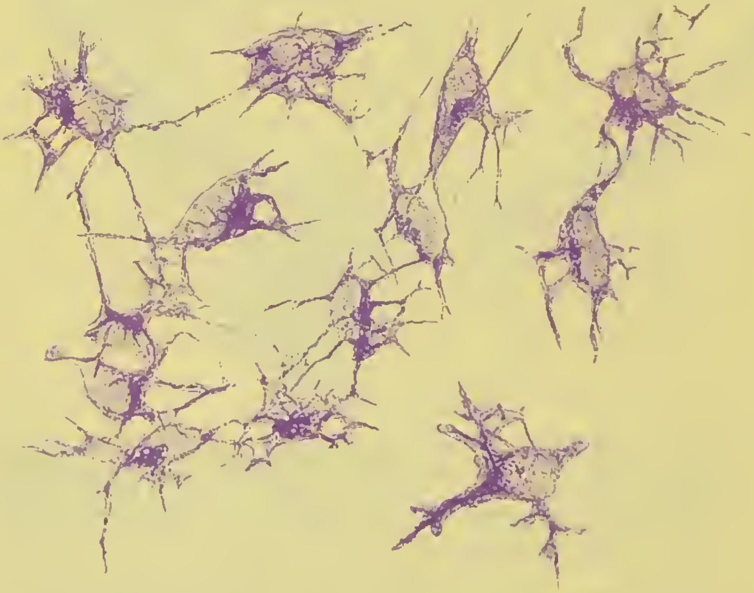


FIG. 590.—CELLS OF CORNEA OF RABBIT STAINED WITH GOLD CHLORIDE. Magnified 300 diameters.

connective-tissue corpuscles (fig. 590), which are branched and united by their processes into a continuous network; there is, of course, a corresponding network of cell-spaces (fig. 591). In vertical sections the cells appear narrow and spindle-shaped. In the superficial laminæ

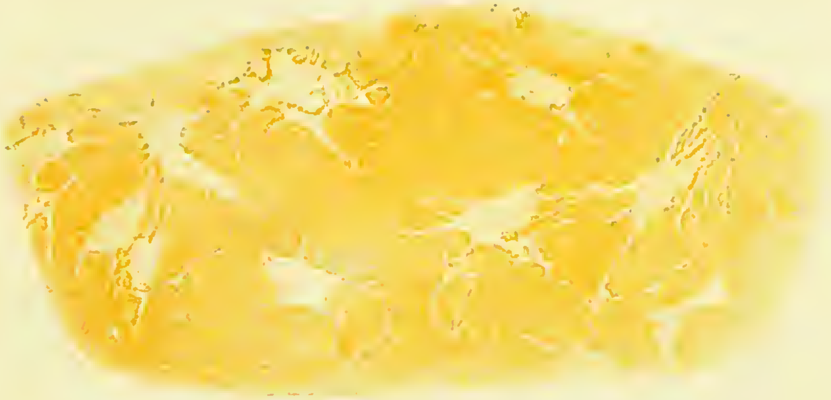


FIG. 591. CELL-SPACES OF CORNEA PREPARED WITH SILVER NITRATE. Magnified 300 diameters. Preparation by H. Pringle.

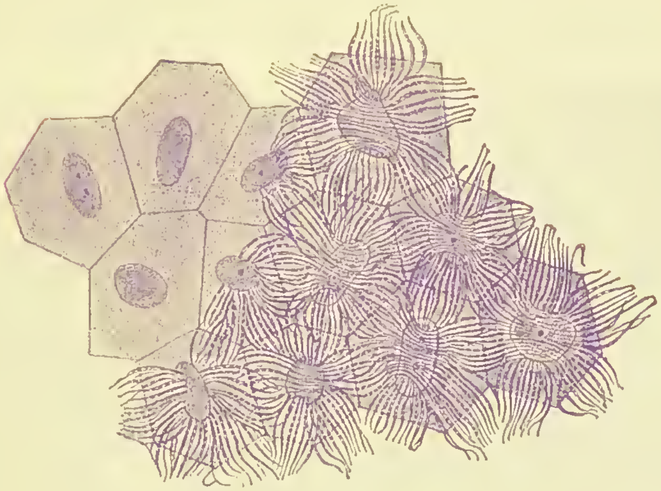


FIG. 592.—EPITHELIUM-CELLS OF DESCEMET'S MEMBRANE. (Smirnow.)

near the margin there are a few bundles of fibres which run obliquely towards the surface (fig. 588, *a*).

4. A homogeneous elastic layer (*membrane of Descemet*). This completely covers the back of the cornea, but near the angle which the cornea forms with the iris it breaks up into separate fibres (*ligamentum*

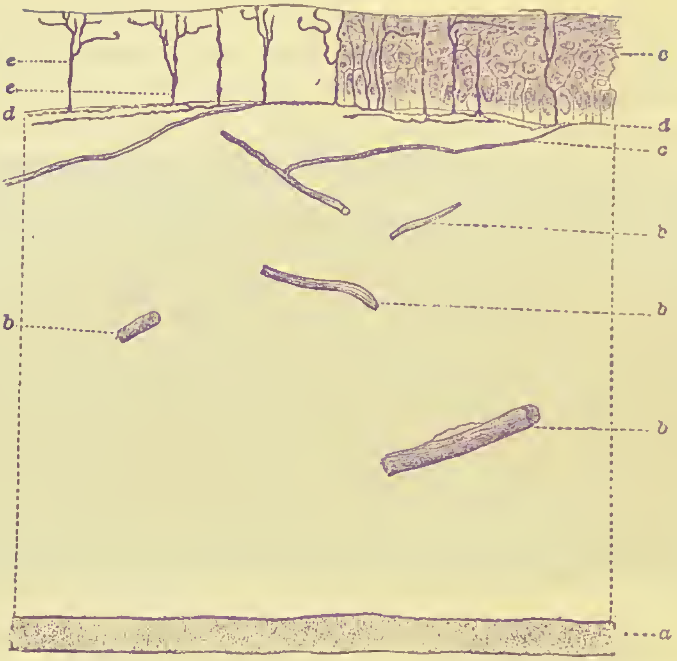


FIG. 593.—VERTICAL SECTION THROUGH THE CORNEA. (Cohnheim.)

The corneal corpuscles and the cells of Descemet's membrane are not represented; the anterior epithelium has been drawn in only in part. *a*, Descemet's membrane; *b*, parts of nerve plexus in substantia propria; *c*, branches going to the epithelium; *d*, fibres of the subepithelial layer; *e*, vertical fibrils with horizontal outrunners.

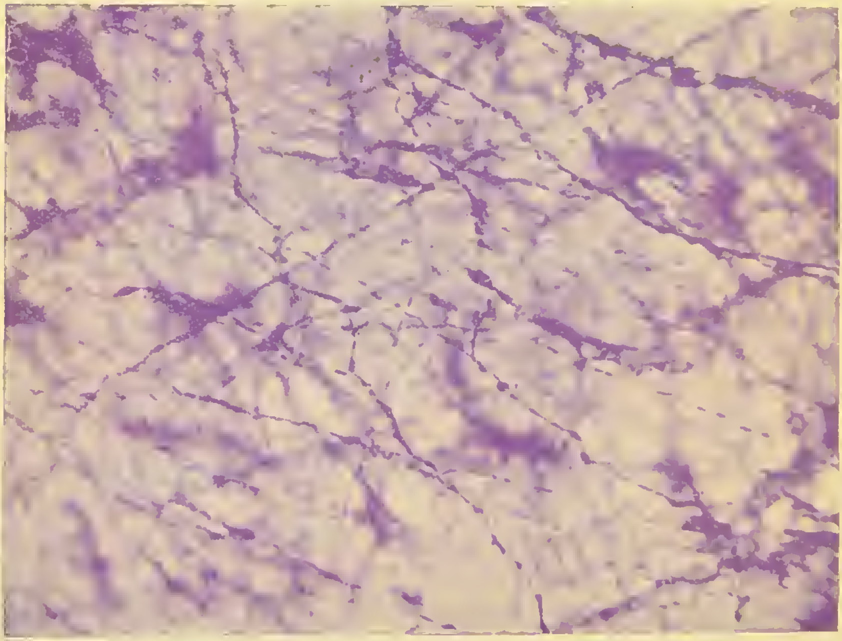


FIG. 594.—CELLS AND NERVE-FIBRILS OF POSTERIOR SURFACE OF FROG'S CORNEA. Gold preparation.

pectinatum) which are partly continued into the iris as the pillars of the iris.

5. A layer of pavement-epithelium (*epithelium of Descemet's membrane*) covering the posterior surface of the elastic lamina, and lining the front of the anterior chamber of the eye (fig. 588, 5). At the sides it is continued over the ligamentum pectinatum into a similar epithelium, covering the anterior surface of the iris. The cells of the epithelium of Descemet's membrane are separated from one another by intercellular spaces, which under favourable circumstances may be seen to be bridged across by bundles of fibrils which pass through the cells (fig. 592).

The nerves of the cornea pass in from the periphery, losing their medullary sheath as they enter the corneal substance. They form a primary plexus in the substantia propria, a secondary or subepithelial plexus immediately under the epithelium which covers the anterior surface, and a terminal plexus of the fine fibrils which pass from the subepithelial plexus in pencil-like tufts and become lost between the epithelium-cells (fig. 593). In some animals (*e.g.* frog) there is also a plexus of fine fibrils near the posterior surface under the epithelium of Descemet's membrane (fig. 594). There are no blood-vessels or lymphatics in the cornea, although they come close up to its margin.

THE CHOROID AND IRIS.

The **choroid** or **vascular coat** of the eye is of a black colour in many animals, but in the human eye it is dark brown. It is composed of connective tissue, the cells of which are large and filled with pigment (figs. 595, 596). It contains in its inner layer a close network of blood-vessels, and in its anterior part the involuntary

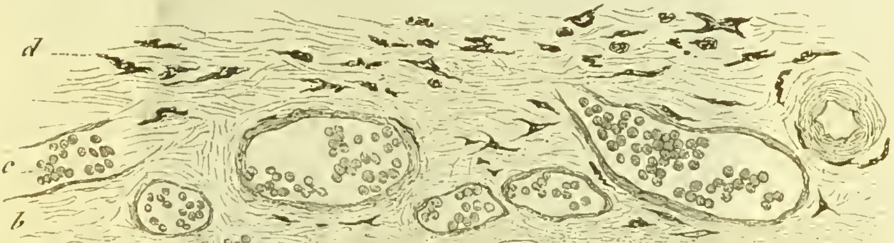


FIG. 595.—SECTION OF CHOROID. (Cadiat.) Diagrammatic.
a, membrane of Bruch: the chorio-capillaris is just above it; *b*, vascular layer; *c*, vessels with blood corpuscles; *d*, lamina suprachoroidea.

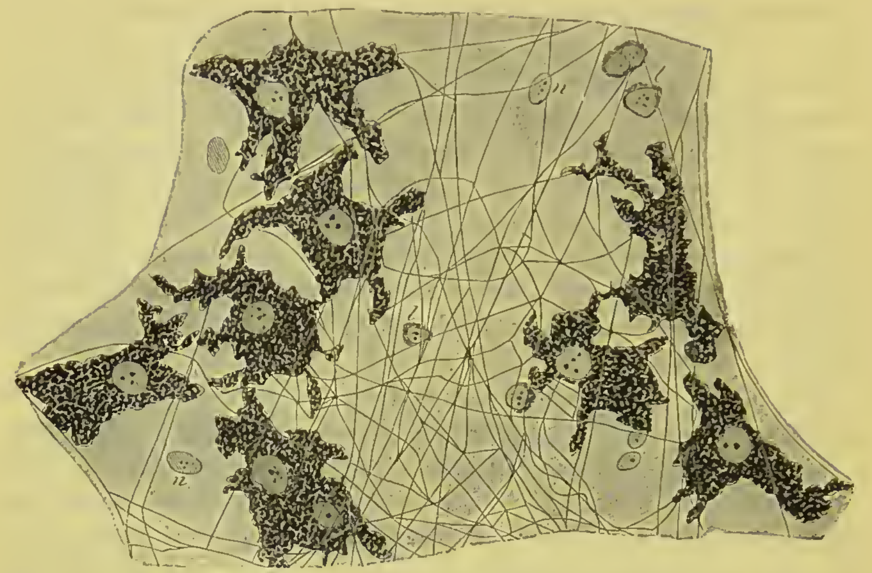


FIG. 596.—A SMALL PORTION OF THE LAMINA SUPRACHOROIDEA. Highly magnified.

The pigment-cells and elastic fibres are well shown ; *n*, nuclei of endothelial cells (the outlines of the cells are not indicated) ; *l*, lymph-cells.

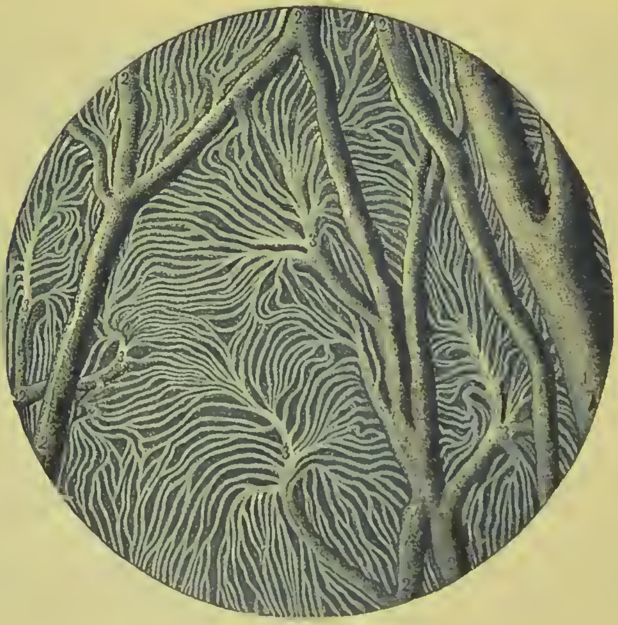


FIG. 597.—INJECTED BLOOD-VESSELS OF THE CHOROID COAT. (Sappey.)

1, one of the larger veins ; 2, small anastomosing vessels ; 3, branches dividing into the smallest vessels.

muscular fibres of the ciliary muscle, which pass backwards from their origin at the junction of the cornea and sclerotic, to be inserted into the choroid. The choroid is separable into the following layers (enumerated from without in):

1. The *lamina suprachoroidea* (fig. 595, *d*). This is a loose membrane composed of delicate connective tissue pervaded by a network of fine elastic fibres, and containing many large branched pigment-cells and lymph-corpuscles (fig. 596). It is covered superficially by a lymphatic endothelium, and is separated from the lamina fusca of the sclerotic by a cleft-like lymph-space which is bridged across here and there by the passage of vessels and nerves, and by bands of connective tissue.

2. The *vascular layer* of the choroid (fig. 595, *b*), which resembles the suprachoroidea in structure, but contains the blood-vessels of the coat. In its outer part are the larger vessels (arteries and veins), the veins having a peculiar vorticose arrangement; in its inner part (chorio-capillaris) are the capillaries, which form an extremely close network with elongated meshes, the capillaries radiating from the extremities of the small arteries and veins in a highly characteristic manner (fig. 597). In the ciliary processes the vessels have for the most part a longitudinal direction, but there are numerous convoluted transversely disposed capillaries uniting the longitudinal vessels (fig. 602, *d*).

3. Lining the inner surface of the choroid is a thin transparent membrane known as the *membrane of Bruch* (fig. 595, *a*).

The **ciliary muscle** consists of involuntary muscular bundles which arise at the corneo-sclerotic junction, and pass meridionally backwards to be inserted in the choroid (fig. 598, *M*). Many of the deeper-seated bundles take an oblique direction, and these pass gradually into others which run circularly around the circumference of the iris, and on a level with the ciliary processes. This set of circularly arranged bundles constitutes the *circular ciliary muscle* of H. Müller (*Mu.*); it is most marked in hypermetropic eyes.

The **iris** is that part of the vascular coat of the eye which extends in front of the lens. It is continuous with the choroid and has a similar structure, but its pigment-cells often contain variously coloured pigment. Besides the delicate connective tissue with numerous elastic fibres and blood-vessels of which it is chiefly composed, it contains two sets of plain muscular fibres. The one set forms the *sphincter* muscle (figs. 598, *s.p.*, 599, *a*), which encircles the pupil; the other set consists of a flattened layer of radiating fibres which extend from the attachment of the iris nearly to the pupil, lying close to the posterior surface and constituting the *dilatator* muscle (fig. 599, *b*; fig. 601).

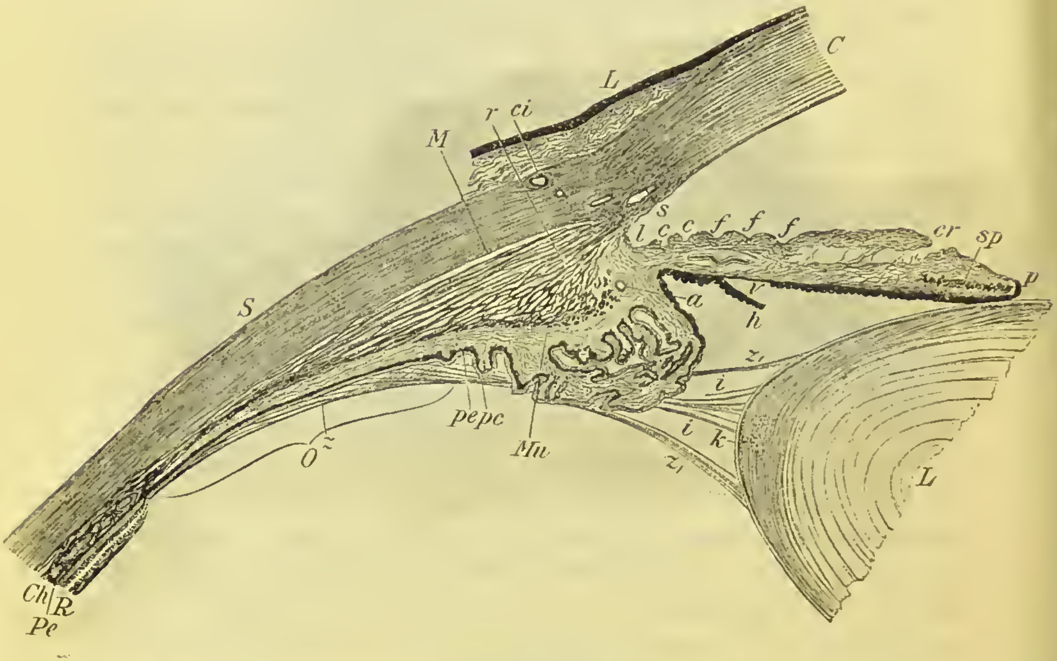


FIG. 598.—SECTION THROUGH THE CILIARY PART OF THE EYE, INCLUDING PART OF THE CORNEA, THE ORA SERRATA, THE IRIS AND THE EDGE OF THE LENS WITH ITS SUSPENSORY LIGAMENT. (Fuchs.)

C, cornea; *S*, sclerotic; *Ch*, choroid; *R*, retina; *Pe*, its pigmented epithelium; *O*, pars ciliaris: this is continued over the choroid processes; *p.e.*, *p.c.*, pigmented and non-pigmented layer of pars ciliaris; *L*, lens; *M*, ciliary muscle; *r*, its radiating (meridional) fibres passing from their origin at the corneo-sclerotic junction; *Mu*, circular ciliary muscle; *ci*, artery of sclerotic; *s*, vein (canal of Schlemm); *z*, fibres of zonula of Zinn passing between choroid processes into the suspensory ligament of the lens (*z′*, *i*); *l*, angle of anterior chamber; *sp*, sphincter pupillæ; *p*, edge of pupil; *h*, pigmented epithelium of iris (accidentally detached at this point and showing, *v*, layer of dilatator pupillæ); *c*, *c*, *f*, *f*, creases and folds of anterior surface of iris; *cr*, a fissure in this surface (accidental); *a*, artery at insertion of iris; *k*, capsule of lens.

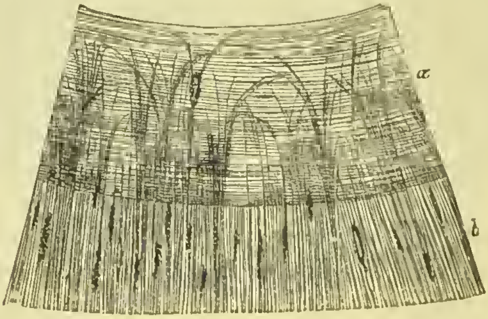


FIG. 599.—SEGMENT OF THE IRIS, SEEN FROM THE POSTERIOR SURFACE AFTER REMOVAL OF THE UVEAL PIGMENT. (Iwanoff.)

a, sphincter muscle; *b*, dilatator muscle of the pupil.

The back of the iris is covered by a thick double layer of pigmented epithelium (uvea) (fig. 601) continuous with the epithelium of the pars ciliaris retinæ (p. 525).

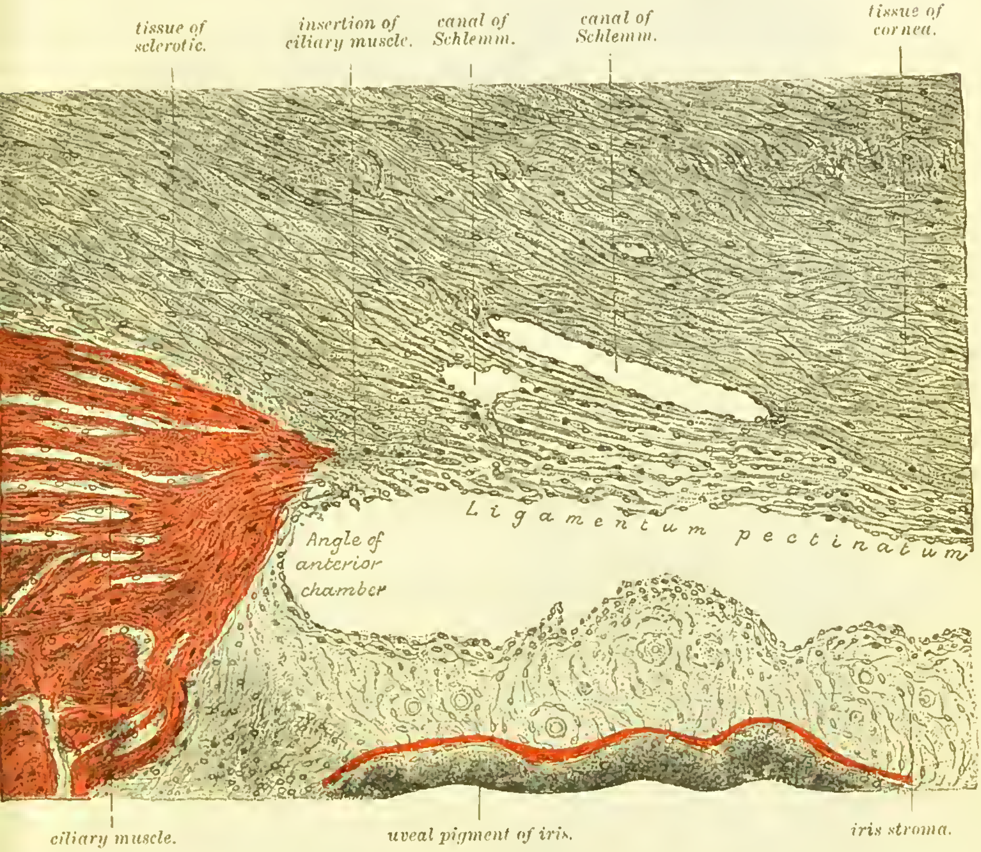


FIG. 600.—SECTION (FROM THE EYE OF A MAN), SHOWING THE RELATIONS OF THE CILIARY MUSCLE TO THE SCLEROTIC, IRIS, AND THE CAVERNOUS SPACES NEAR THE ANGLE OF THE ANTERIOR CHAMBER.

The figure, which is copied from a photograph, includes only a small portion of the ciliary muscle, the fibres of which are seen to be converging to a point immediately anterior to the angle of the anterior chamber. Here they are attached through the medium of a tongue of fibrous tissue of the sclerotic (consisting mainly of circular bundles) to the outer part of the ligamentum pectinatum, which forms a loose tissue with open meshes lying between the canal of Schlemm and the anterior chamber. To the right of the figure the fibres of the ligamentum pectinatum are seen to be gradually converging towards the posterior surface of the cornea, and somewhat beyond the part shown in this figure they merge into the membrane of Descemet. A communication of the canal of Schlemm, which is double in this section, with the endothelial-lined spaces in the ligamentum pectinatum, is seen, and also communications between the last-named spaces and the anterior chamber.

The muscular tissue of the iris is developed from the epithelium at the back of the iris (Nussbaum, Szili).

The blood-vessels of the iris (fig. 602, *e*) converge towards the pupil. Near the pupil the small arteries form an anastomotic circle, from which capillaries arise and pass still nearer the pupil, around which they form a close capillary network.

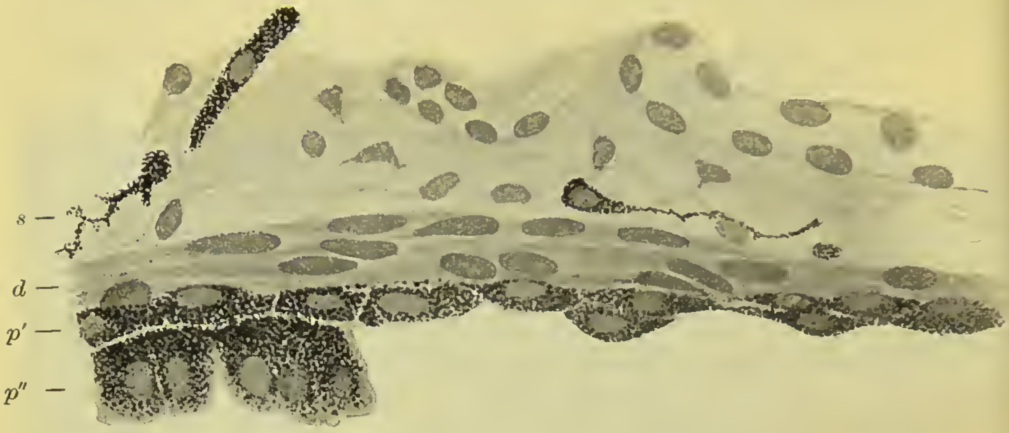


FIG. 601.—SECTION OF POSTERIOR LAYERS OF HUMAN IRIS, NEAR ITS ATTACHMENT TO THE CHOROID. Magnified 600 diameters.

s, iris stroma, with connective tissue, branched pigment-cells, and blood-vessels; *d*, dilatator muscle; *p*′, deeper layer of uveal pigment; *p*″, superficial layer of uveal pigment: this layer is broken away from the larger part of the section.

A large number of nerve-fibres are distributed to the choroid and iris, probably going chiefly to the muscular tissue of those parts (ciliary muscle and sphincter and dilatator pupillæ).

THE RETINA.

The **retina** consists of the eight layers shown in the accompanying diagram (fig. 603), numbered as they occur from within out.

The inner surface of the retina, which is smooth, rests upon the hyaloid membrane of the vitreous humour. It is formed of the united bases of the fibres of Müller, which will be afterwards described.

The *layer of nerve-fibres* is formed by the expansion of the optic nerve after it has passed through the coats of the eye (fig. 604). The optic nerve differs from other cerebro-spinal nerves in being made up not of separate cylindrical bundles or funiculi, but of one large bundle, covered with a thick sheath and subdivided by numerous interlacing septa into portions of irregular size and shape (fig. 604). A section across the nerve taken near its entrance into the globe shows a central strand of connective tissue containing the central retinal artery and vein which pass obliquely into the nerve a few millimetres from the back of the eye-ball. The sheath of the nerve has a composite structure, being formed externally of a thick fibrous membrane continuous centrally with the dura mater and peripherally with the sclera, internally of a membrane continuous centrally with the pia mater, whilst between the two is a space containing a prolongation of the arachnoid, the space itself being continuous with the subdural and subarachnoid spaces of the cranial cavity. The nervous tissue is greatly diminished

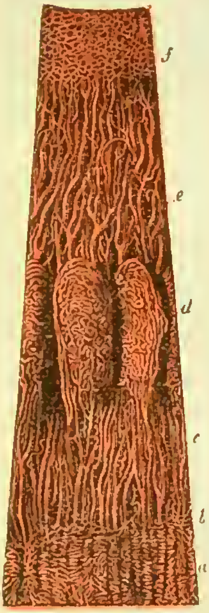


FIG. 602.—VESSELS OF THE CHOROID, CILIARY PROCESSES AND IRIS OF A CHILD. (Arnold) 10 diameters.

a, capillary network of the posterior part of the choroid, ending at *b*, the ora serrata; *c*, arteries of the corona ciliaris, supplying the ciliary processes, *d*, and passing into the iris, *e*; *f*, the capillary network close to the papillary margin of the iris.

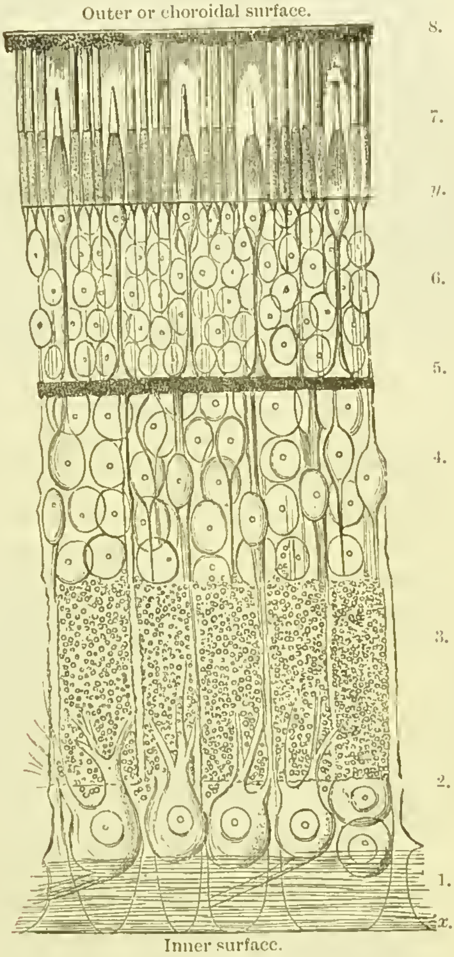


FIG. 603.—DIAGRAMMATIC SECTION OF THE HUMAN RETINA. (M. Schultze.)

1, Layer of optic nerve-fibres; 2, layer of optic nerve-cells; 3, inner synapse (molecular) layer; 4, inner nuclear (bipolar) layer; 5, outer synapse (molecular) layer; 6, outer nuclear layer; 7, layer of rods and cones; 8, layer of pigment-cells; *x*, membrana limitans interna; *y*, membrana limitans externa.

at the lamina cribrosa owing to the disappearance of the medullary sheath of the nerve-fibres, which are continued into the retina as axis-cylinders only.

At its entrance the nerve forms a slight eminence (*colliculus nervi optici*). The nerve-fibres lose their medullary sheath on reaching the retina. Most are connected with (derived from) the cells of the ganglionic or optic nerve-cell layer (fig. 606), but some (centrifugal) fibres pass through the ganglionic and molecular layers to form a terminal arborisation in the inner nuclear layer (fig. 609, *J*, and fig. 607). The layer of nerve-fibres becomes gradually thinner in the anterior part of the retina.

The *layer of optic nerve-cells*, or *ganglionic layer*, is composed of nerve-cells somewhat like the cells of Purkinje of the cerebellum but varying in size, although those of large size are prevalent in most parts of the retina. In the yellow spot, on the other hand, smaller nerve-cells are met with, and they may here lie several deep. These nerve-cells have a fine axis-cylinder process prolonged into a fibre of the layer just noticed and a thick branching process, the ramifications of which terminate in the next layer in flattened arborisations at different levels (fig. 608, A, B, C).

The *inner synapse layer* or *inner molecular layer* is comparatively thick, and has an appearance very like parts of the grey matter of the nerve-centres. A few nuclei are scattered through it, and it is occupied by the processes of the nerve-cells and of the inner granules (bipolars and amacrine cells) which form synapses in it; it is also traversed by the centrifugal fibres from the optic nerve layer, as well as by the fibres of Müller.

The *inner granule layer* (also termed *inner nuclear layer*) is mainly composed of bipolar nerve-cells containing large nuclei. A process (the axon) of each of these cells (fig. 606) extends inwards into the inner molecular layer where it spreads out into a terminal arborisation. These arborisations occur at different levels in the layer, forming synapses with the optic nerve-cells. Another process (dendron) is directed outwards, and arborises in the outer molecular layer, where it forms synapses with the terminations of the rod- and cone-fibres. It has been shown by Ramón y Cajal that there are two kinds of bipolars, one kind (*rod-bipolars*, fig. 606, *c.d.*) being connected externally with the rods of the retina, and passing inwards to ramify over the bodies of the nerve-cells, whereas those of the other kind (*cone-bipolars*, *e*) are connected with the cone-fibres, and ramify in the middle of the inner molecular layer. The outwardly directed processes of these cone-bipolars are, in some animals, but not in mammals,

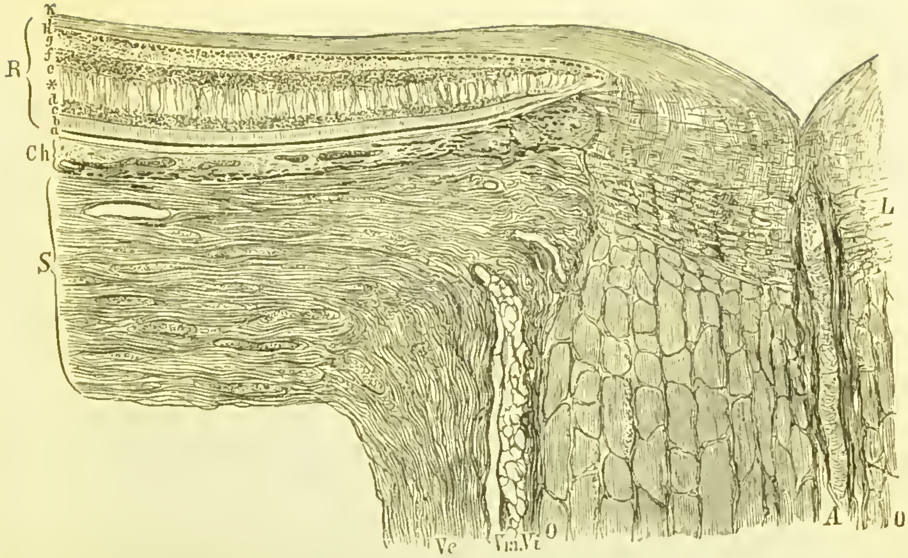


FIG. 604.—SECTION THROUGH THE COATS OF THE EYEBALL AT THE POINT OF ENTRANCE OF THE OPTIC NERVE. (Toldt.)

Ve, dural sheath; *Vm*, arachnoidal sheath, and *Vi*, pia-matral sheath of the optic nerve, with lymphatic spaces between them; *O*, *O*, funiculi of the nerve; *L*, lamina cribrosa; *A*, central artery; *S*, sclerotic; *Ch*, choroid; *R*, retina. The small letters refer to the various parts of the retina, *b* being the layer of rods and cones, and *i* that of nerve-fibres.

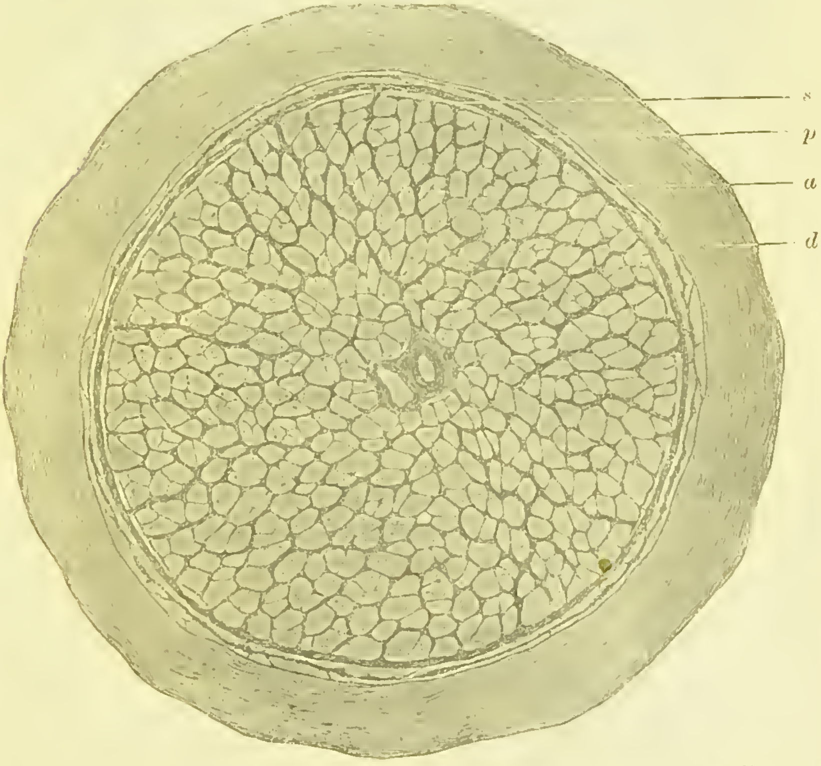


FIG. 605.—SECTION OF OPTIC NERVE: MAN. (Greeff). Magnified 24 diameters.

The sectionis taken near the junction with the globe. *d*, sheath derived from dura; *a*, from arachnoid; *p*, from pia mater; *s*, a layer of superficial neuroglia.

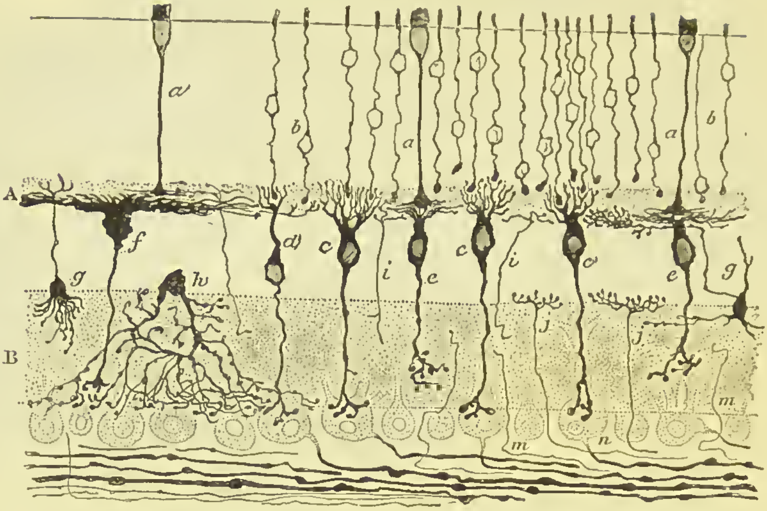


FIG. 606.—SECTION OF DOG'S RETINA, GOLGI METHOD. (Cajal.)

a, cone-fibre; *b*, rod-fibre and nucleus; *c*, *d*, bipolar cells (inner granules) with vertical ramifications of their outer processes or dendrons: in the centre of the ramification lie the enlarged ends of rod-fibres; *e*, other bipolars with flattened ramifications abutting against ramified ends of cone-fibres; *f*, large bipolar with flattened ramification; *g*, inner granule-cell sending an axon towards the rod- and cone-fibres; *h*, amacrine cell with diffuse arborisation of its processes in inner molecular layer; *i*, *j*, *m*, nerve-fibrils passing respectively to outer molecular, inner nuclear, and inner molecular layers; *n*, ganglionic cells, with axons passing into nerve-fibre layer.

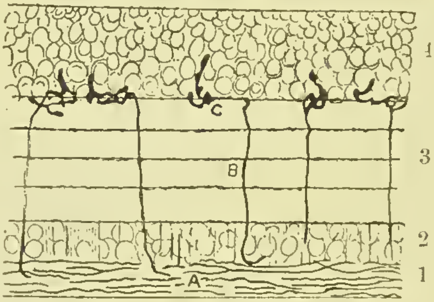


FIG. 607.—SECTION THROUGH THE INNER LAYERS OF THE RETINA OF A BIRD, PREPARED BY GOLGI'S METHOD. (Cajal.)

A, nerve-fibres of optic nerve layer; B, some of these fibres passing through the inner molecular layer to end in an arborisation at the junction of the inner molecular and inner nuclear layers. The layers in this and in the two succeeding cuts are numbered in correspondence with the layers in fig. 603.

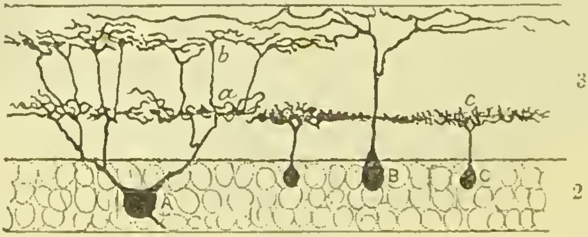


FIG. 608.—SECTION ACROSS THE MOLECULAR AND GANGLIONIC LAYERS OF BIRD'S RETINA, PREPARED BY GOLGI'S METHOD. (Cajal.)

Three or four ganglionic cells, A, B, C, and the terminal arborisations of their dendrons, *a*, *b*, *c*, in the molecular layer, are shown.

continued on as far as the external limiting membrane, where each ends in a free extremity (*fibre of Landolt*, fig. 609, E). Besides these bipolar nerve-cells, there are other larger inner granules (spongioblasts of some authors) which are different in character, having ramified processes which extend into the inner molecular layer (figs. 606, *h*; 609, A, B, C), in which the bodies of these cells are often partly imbedded. The cells in question have been regarded as of the nature of neuroglia-cells, but according to Cajal they are probably all nerve-cells. He has termed them *amacrine-cells*, from the fact that they were believed to be destitute of a long process; but some have been noticed to give off, besides the branching processes or dendrons, which ramify in the molecular layer, an axis-cylinder process which may extend into the nerve-fibre layer. There are also some cells in the outer part of the granule layer which send their processes entirely into the outer molecular layer (fig. 609, H). These are the *horizontal-cells* of Ramón y Cajal (termed spongioblasts of outer molecular layer by some authors). The fibres of Müller have nucleated enlargements (fig. 609, J) in the inner nuclear layer.

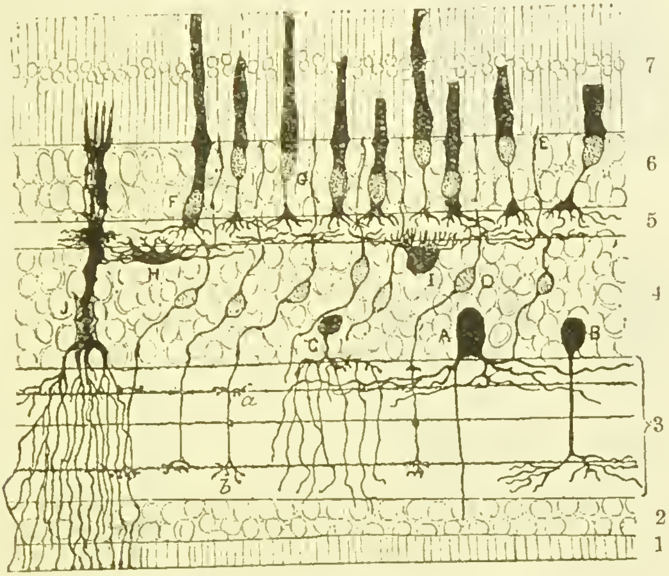


FIG. 609.—SECTION OF BIRD'S RETINA, PREPARED BY GOLGI'S METHOD. (Cajal.)

A, large nerve-cell of inner nuclear layer; B, C, amacrine cells; D, small bipolar nerve-cells with one process, ramifying in the inner molecular layer and the other one ramifying in the outer molecular layer, and extending (E) as far as the rods and cones as a fibre of Landolt; F, G, rod- and cone-nuclei respectively; H, I, cells with dendrons ramifying in outer molecular layer; J, fibre of Müller.

The *outer molecular layer* is thin, and is composed mainly of the arborisations of the inner granules, of the rod- and cone-fibres, and of the horizontal cells (figs. 606, 609), which all form synapses in this layer.

The *outer nuclear layer* and the *layer of rods and cones* are composed of elements which are continuous through the two layers, and they should properly, therefore, be described as one. It has been termed the *sensory epithelium of the retina* (fig. 610, 6 and 7). The elements of which this nerve-epithelium consists are elongated nerve-cells of two kinds. The most numerous, which may be termed the *rod-elements*, consist of peculiar rod-like structures (*retinal rods*) set closely side by side, each of which is prolonged internally into a fine varicose fibre (*rod-fibre*) which swells out at one part of its course into a nucleated enlargement, and ultimately ends (in mammals) in a minute knob within the outer molecular layer, where it is imbedded in the ramifications of the dendrons of the rod-bipolars. The rod consists of two segments, an outer cylindrical and transversely striated segment, which during life has a purplish-red colour if the eye has not been recently exposed to light and an inner slightly bulged segment which in part of its length is longitudinally striated. The nucleus of the rod-element in some animals, but according to Flemming not in man, has a transversely shaded aspect in the fresh condition (fig. 610). The *cone-elements* are formed of a conical tapering external part, the *retinal cone*, which is directly prolonged into a nucleated enlargement, from the farther side of which the *cone-fibre*, considerably thicker (in mammals) than the rod-fibre, passes inwards, to terminate by an expanded arborisation in the outer molecular layer; here it comes into relation with a similar arborisation of dendrons of a cone-bipolar. The cone, like the rod, is formed of two segments, the outer of which, much the smaller, is transversely striated; the inner, bulged segment being longitudinally striated. The inner ends of the rod- and cone-fibres, as already stated, form synapses with the peripheral arborisations of the bipolars, and through

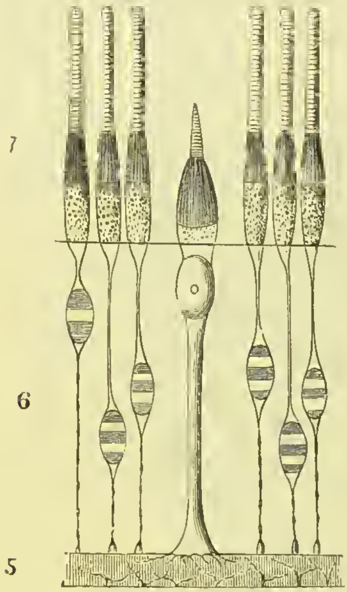


FIG. 610.—DIAGRAMMATIC REPRESENTATION OF THE ROD- AND CONE-ELEMENTS OF THE RETINA. (After Schwalbe.)

The designation of the numbers is the same as in fig. 603.

the latter elements and their synapses in the inner molecular layer a connection is brought about with the nerve-cells and nerve-fibres of the innermost layers. The connection of the retinal elements with one another and through the optic fibres with the central nervous system (anterior corpora quadrigemina and lateral geniculate bodies) is shown diagrammatically in fig. 611.

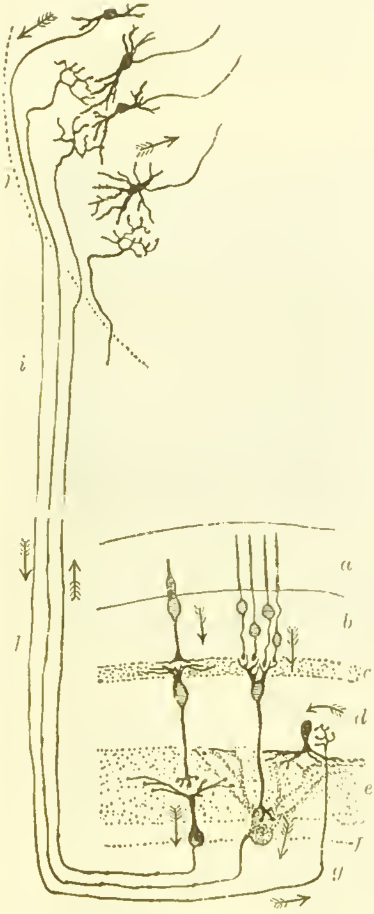


FIG. 611.—DIAGRAM OF THE CONNECTIONS OF THE RETINAL ELEMENTS WITH ONE ANOTHER AND WITH THE CENTRAL NERVOUS SYSTEM. (Cajal.)

a to *g*, layers of retina; *a*, rods and cones; *b*, outer nuclear layer; *c*, outer molecular layer; *d*, inner nuclear layer; *e*, inner molecular layer; *f*, nerve-cells giving origin to fibres of optic nerve; *g*, *h*, *i*, a centrifugally conducting fibre, with a terminal arborescence in the retina; *j*, grey matter of corpus geniculatum or corpus quadrigeminum.

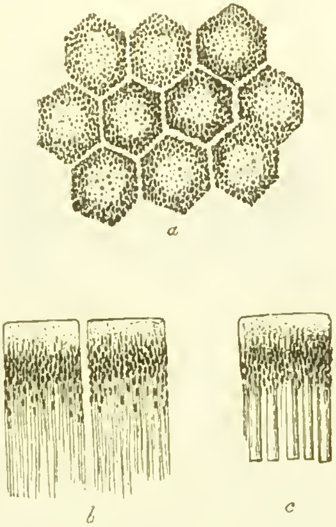


FIG. 612.—PIGMENTED EPITHELIUM OF THE HUMAN RETINA. (M. Schultze.) Highly magnified.

a, cells seen from the outer surface with clear lines of intercellular substance between; *b*, two cells seen in profile with fine offsets extending inwards; *c*, a cell still in connection with the outer ends of the rods.

In birds, reptiles, and amphibia a small oil-globule, often brightly coloured red, yellow, or green, is found in the inner segment of each cone. Other variations of structure are met with in different animals.

The cones are most numerous at the back of the retina; they are fewer in number, and the rods are proportionally more numerous towards the anterior part.

The *pigmentary layer* forms the most external part of the retina. It consists of hexagonal epithelium-cells (fig. 612), which are smooth externally where they rest against the choroid, but are prolonged internally into fine filaments which extend between the rods. The pigment-granules, many of which are in the form of minute crystals, lie in the inner part of the cell, and after prolonged exposure to light they are found extending along the cell-processes between the rods (Kühne), their function being probably connected with the restoration of the purple colouring matter which has been bleached by the light. This extension of the pigment is accompanied by a shortening of the cones (Engelmann) (fig. 613).

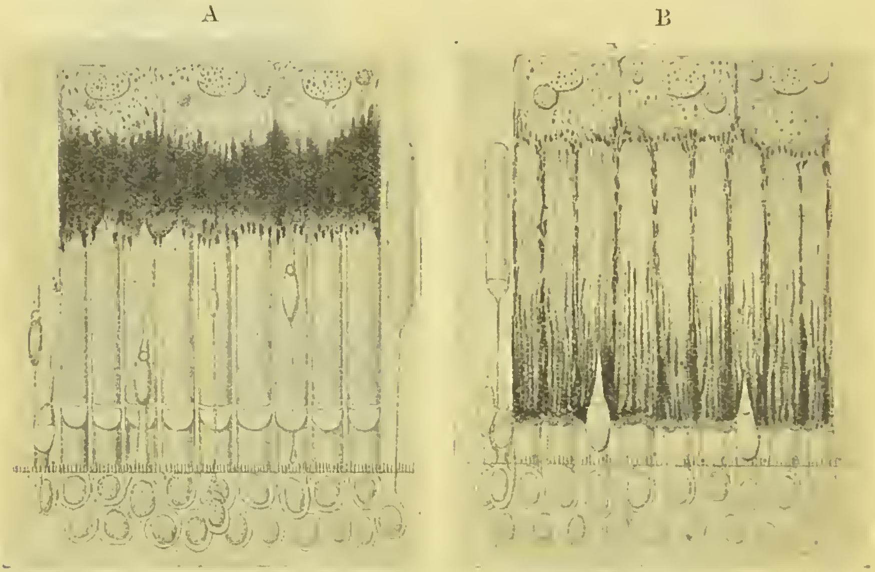


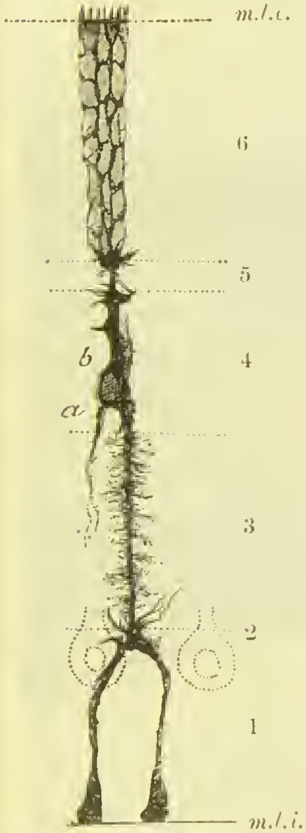
FIG. 613.—A. PART OF A SECTION OF THE RETINA FROM THE EYE OF A FROG WHICH HAD BEEN KEPT IN THE DARK FOR SOME HOURS BEFORE DEATH. (v. Genderen-Stort.)

The pigment is collected towards the outer ends of the rods, which were red, except the outer detached rod, which was green. The cones, which in the frog are much smaller than the rods, are mostly elongated.

B. A SIMILAR SECTION FROM A FROG WHICH HAD BEEN EXPOSED TO LIGHT.

The pigment is extended between the rods, and is accumulated near their bases. The rods were colourless. All the cones are contracted.

Fibres of Müller.—The fibres of Müller (fig. 609, *J*, and fig. 614) are long stiff cells which pass through several of the retinal layers. Commencing at the inner surface of the retina by expanded bases which unite with one another to form the so-called internal limiting membrane (fig. 615), they pass through all the layers in succession, until they reach the outer granule layer. Here they branch and expand into a sort of honeycomb tissue which serves to support the fibres and nuclei of the rod- and cone-elements. At the bases of the rods and cones, this sustentacular tissue ceases, being here bounded by a distinct margin which has been called the external limiting membrane



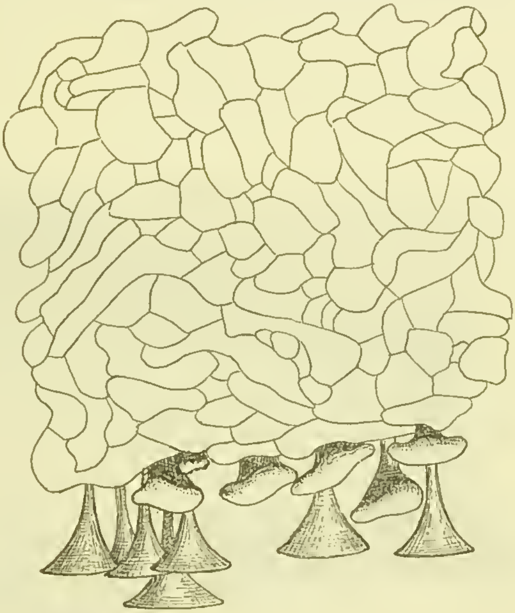


Fig. 615.

Fig. 614.—A fibre of Müller from the dog's retina, Golgi method. (Cajal).

1, nerve-fibre layer; 2, nerve-cell layer; 3, inner molecular layer; 4, inner granule layer; 5, outer molecular layer; 6, outer granule layer; *b*, nucleus of the fibre; *a*, a process extending into inner molecular layer; *m.l.i.*, membrana limitans interna; *m.l.e.*, membrana limitans externa.

Fig. 615.—Internal limiting membrane of retina treated with silver nitrate, showing the outlines of the bases of the fibres of Müller. (G. Retzius.)

Fig. 614.

(fig. 614, *m.l.e.*), but delicate sheaths pass from it around the bases of the rods and cones. Each Müllerian fibre, as it passes through the inner granule layer, has a nucleated enlargement (*b*), indicating the cell nature of the fibre. The fibres of Müller represent ependyma-cells or perhaps long neuroglia-cells such as are found in some parts of the nerve-centres, *e.g.* the cerebellum (see fig. 566).

There are two parts of the retina which call for special description.

The **macula lutea (yellow spot)**, with its **central fovea**, is the part of the retina which is immediately concerned in direct vision. It is characterised firstly by its greater thickness (except at the middle of the fovea), secondly by the large number of its ganglion-cells, which are rounded or conical, and thirdly by the large number of cones it contains as compared with the rods. In the central fovea itself (fig. 616) there are no rods, and the cones are very long and slender, measuring not more than 2μ in diameter; all the other layers become gradually thinned down almost to complete disappearance, so that the middle of the central fovea is the thinnest part of the retina. Since there are few rods, the outer granule layer loses in great measure its appearance of being composed of closely packed nuclei, and the cone-fibres are very distinct, forming the so-called *fibrous layer*. The direction of these fibres is for the most part very oblique in this part of the retina.

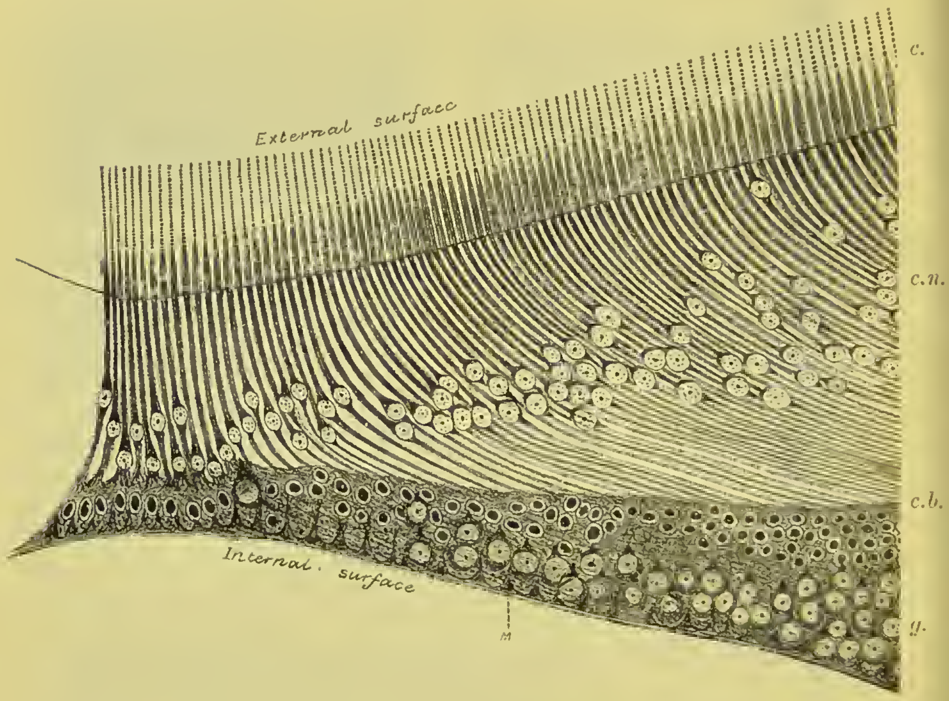


Fig. 616.—Section through the central part of the fovea centralis. $\frac{350}{1}$. (From a preparation by C. H. Golding-Bird.)

M, bases of Müllerian fibres; *c.b.*, nuclei of inner granules (bipolars); *c.n.*, cone-fibre nuclei; *c*, cones.

The pigmentary layer is thickened over the fovea, and there is also a thickening in the choroid coat here, due to a large accumulation of capillary vessels.

The **pars ciliaris retinæ**, which commences at the *ora serrata*, where the retina proper abruptly ends (fig. 617), is composed of two epithelial layers and has no nervous structures. Of the two layers, the external is a thick stratum of pigmented epithelium formed of rounded cells and continuous with the pigmentary layer of the retina on the one hand, and with the uvea of the iris on the other; the inner is a layer of columnar cells, each containing an oval nucleus. These cells probably represent the Müllerian fibres of the retina.

The retina contains relatively few blood-vessels. The central artery enters and the vein leaves it in the middle of the optic nerve. The larger vessels ramify in the nerve-fibre layer, and there are capillary net-works in this layer and in the inner nuclear layer. There are perivascular (lymph) spaces around the veins and capillaries. The sensory epithelium receives no blood-vessels, but is nourished from the vessels of the choroid.

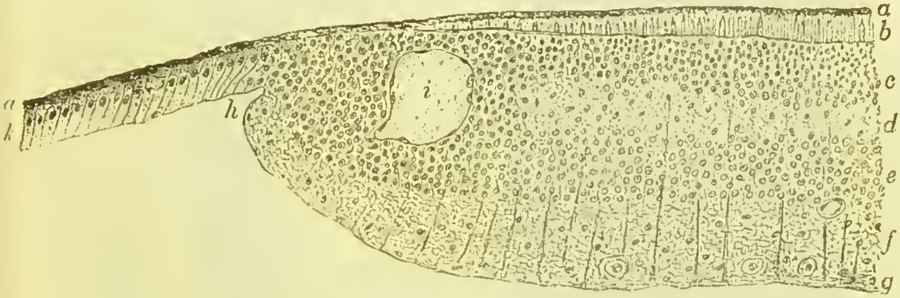


FIG. 617.—SECTION OF HUMAN RETINA AT ORA SERRATA, SHOWING THE ABRUPT TERMINATION OF THE USUAL RETINAL LAYERS AND THE CONTINUATION OF THE RETINAL SHEET AS TWO LAYERS OF CELLS, WHICH FORM THE PARS CILIARIS RETINÆ. (Piersol.)

a, *a*, pigment layer; *b*, rod- and cone-layer; *c*, outer nuclear layer; *d*, outer molecular layer; *e*, inner nuclear layer; *f*, inner molecular layer; *g*, ganglion-cell and nerve-fibre layers; *h*, section at transition line; *k*, columnar cells of pars ciliaris; *i*, a cyst (such cysts occur occasionally here).

THE LENS AND VITREOUS HUMOUR.

The lens.—The lens is a laminated fibrous body inclosed by a transparent elastic capsule to which, around the circumference, the fibres of the suspensory ligament are attached (fig. 598). Immediately within the capsule, in front and at the sides, there is a layer of cubical epithelium termed the epithelium of the capsule, but at the margin of the lens the cells become longer and pass by a gradual transition into the lens-fibres (fig. 618). The *fibres* which compose the lens are long and

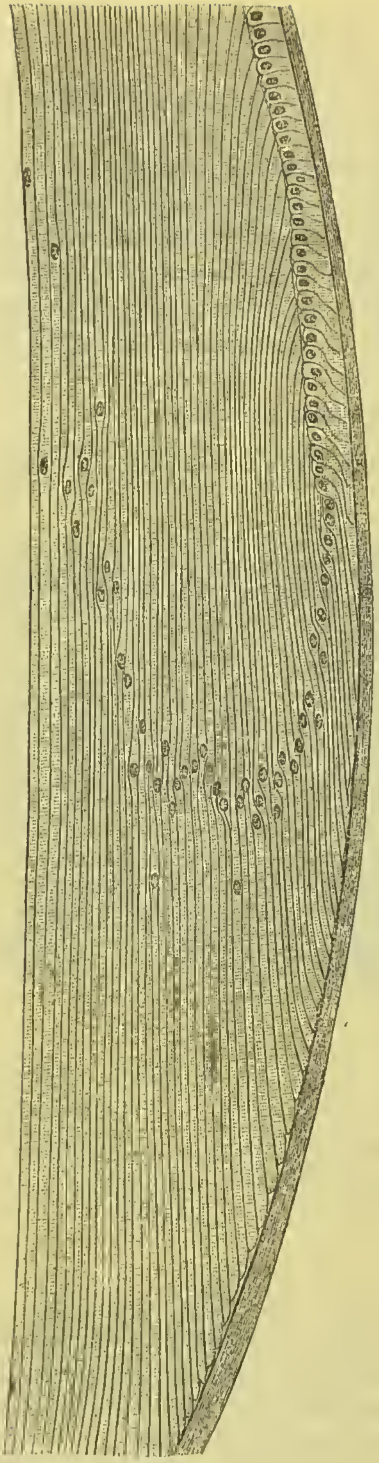


Fig. 618.—Section through the margin of the rabbit's lens, showing the transition of the epithelium of the capsule into the lens-fibres. (Babuchin.)

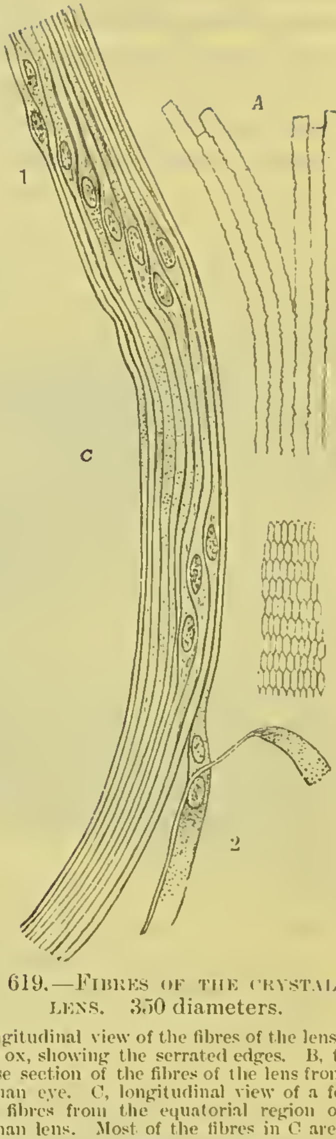


Fig. 619.—Fibres of the crystalline lens. 350 diameters.

A, longitudinal view of the fibres of the lens from the ox, showing the serrated edges. B, transverse section of the fibres of the lens from the human eye. C, longitudinal view of a few of the fibres from the equatorial region of the human lens. Most of the fibres in C are seen edgewise, and, towards 1, present the swellings and nuclei of the 'nuclear zone'; at 2, the flattened sides of two fibres are seen. (A and B from Kölliker: C from Henle.)

riband-shaped, with finely serrated edges (fig. 619, A); in transverse section they appear prismatic (B). Many of the superficial fibres are nucleated (C), the lens-fibres having originally been developed by the elongation of epithelium-cells.

The vitreous humour.—This is composed of soft gelatinous tissue, apparently structureless when examined in the fresh condition, but containing fibres and a few scattered cells, the processes of which are often long and varicose, and the cell-bodies distended by large vacuoles (fig. 620). The *hyaloid membrane*, which invests the vitreous humour, is homogeneous and structureless except in the region of the ciliary processes, where it is fibrous in structure, forming the zonule of Zinn and spreading out into the suspensory ligament of the lens (fig. 598). This part of the hyaloid membrane is connected with a circular fibrous portion of the vitreous humour which serves to give additional firmness to the attachment of the fibres of the suspensory ligament of the lens (Anderson Stuart).

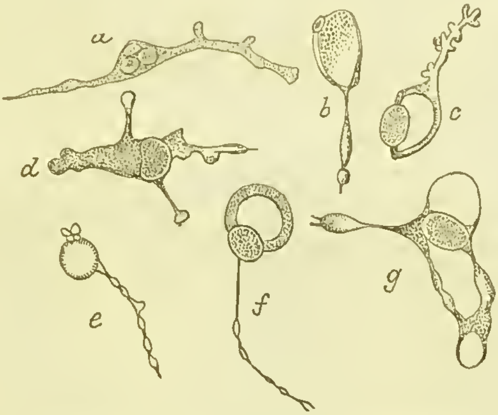


FIG. 620.—CELLS OF VITREOUS. (Schwalbe.)

a, *d*, without vacuoles; *b*, *c*, *e*, *f*, *g*, with vacuoles.

LESSON XLIX.

STRUCTURE OF THE OLFACTORY MUCOUS MEMBRANE AND OF THE EXTERNAL AND MIDDLE EAR.

1. Vertical sections of the nasal mucous membrane. The sections may be carried either across the upper turbinate bone, after decalcification, or across the upper part of the nasal septum. Make a sketch under the low power. Notice the difference in the character of the epithelium in the olfactory and respiratory parts of the membrane.

2. Teased preparation of the epithelium of the olfactory mucous membrane. A piece of the membrane is placed quite fresh in osmic acid (1 per cent.) for a few hours, and is then macerated for two days or more in water. The epithelium is broken up in dilute glycerine; the cells easily separate from one another on tapping the cover-glass. Notice the two kinds of cells. Sketch some of the cells under a high power.[1]

3. Sections of the external ear (these have been already studied for the cartilage, Lesson XII.).

4. Sections across the cartilaginous part of the Eustachian tube. Sketch under the lower power.

5. Preparation of the membrana tympani. A piece of the membrane, stained with magenta and gentian violet (see Lesson IX., § 2), is mounted flat in xylol balsam or dammar.

Determine the composition of the membrane—*i.e.* the several layers composing it—by focussing carefully with the high power.

THE OLFACTORY MUCOUS MEMBRANE.

The **olfactory region** of the nasal fossæ includes the upper and middle turbinate processes and the upper third of the septum. It is covered by a soft vascular mucous membrane of a yellow colour in man.

The *epithelium* of the olfactory mucous membrane (figs. 621, 622) is very thick and is composed of long cells, set closely side by side and bounded superficially by a cuticular lamina, through which the free ends of the cells project. The cells are of two kinds: 1. Long narrow spindle-shaped or bipolar nerve-cells consisting of a larger part or body (*b*) containing the nucleus, and of two processes or poles, one (*c*) straight and cylindrical and extending to the free surface, the other (*d*) very delicate and varicose, looking not unlike a nerve-fibril and extending down towards the corium. The position of the nuclear enlargement varies, and with it the relative length of the two processes. The distal or free process terminates in a small clear projection, which passes beyond the cuticular membrane; in amphibia, reptiles, and birds, and perhaps also in mammals, it bears fine stiff hair-like filaments. The proximal or varicose process becomes lost amongst the plexus of olfactory nerve-fibres, at the base of the epithelium; it is connected with one of these fibres, and ultimately passes through the cribriform plate of the ethmoid to end in an arborisation within one of the olfactory glomeruli (see diagram, fig. 582, p. 496). These cells have been termed the *olfactory cells*. 2. Long columnar epithelium-cells (*a*), with comparatively broad cylindrical nucleated cell-bodies placed next to the free surface, and long, forked, and branching tail like processes extending down to the corium. These are regarded not as sensory epithelium-cells, but merely as serving to support the proper olfactory cells. They are the *columnar* or *sustentacular cells*. 3. Tapering cells are present, at least in some animals, in the deeper part of the epithelium. They rest by their bases upon the corium, and project between the other cells, which they assist to support.

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[1] The connection of the olfactory cells with the olfactory nerve-fibres is displayed in embryos, the method of Golgi being employed.

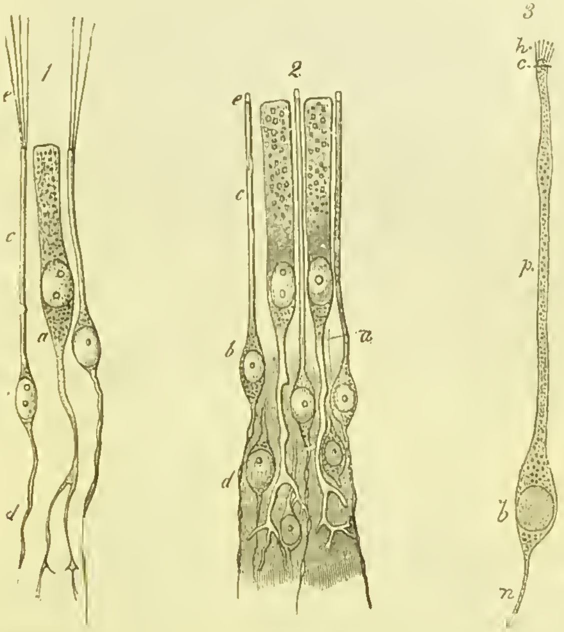

FIG. 621.—CELLS AND TERMINAL NERVE-FIBRES OF THE OLFACTORY REGION. Highly magnified.

1, from the frog; *2* and *3*, from man. In *1* and *2*:—*a*, epithelial cell, extending deeply into a ramified process; *b*, olfactory cells; *c*, their peripheral rods; *e*, the extremities of these, seen in *1* to be prolonged into fine hairs; *d*, their central filaments. In *3*:—*h*, hairlets; *c*, free border of cell; *p*, peripheral process; *b*, body of cell; *n*, nerve-fibre. *1* and *2* from M. Schultze; *3*, from v. Brunn.

The *corium* of the olfactory mucous membrane is also very thick (fig. 622). It contains numerous blood-vessels, bundles of the olfactory nerve-fibres (which are non-medullated), and a large number of serous glands known as *Bowman's glands* (*b*), which open upon the surface by ducts which pass between the epithelium-cells.

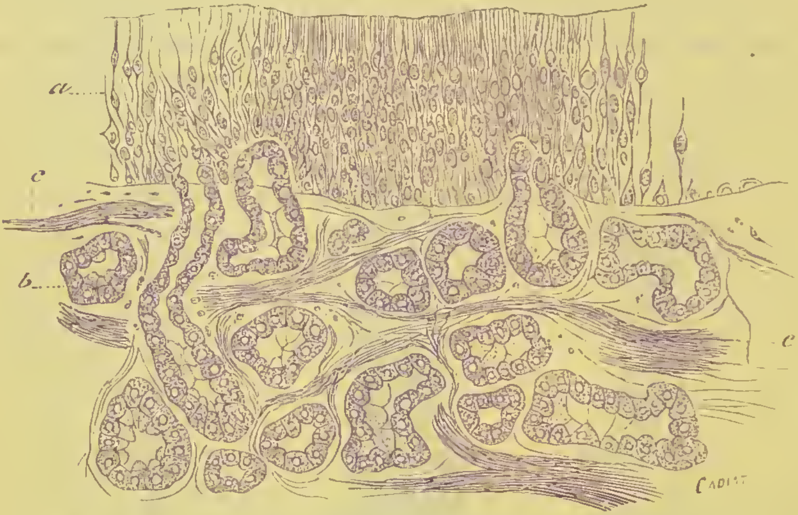

FIG. 622.—SECTION OF OLFACTORY MUCOUS MEMBRANE. (Cadiat.)
a, epithelium ; *b*, glands of Bowman ; *c*, nerve-bundles.

THE EXTERNAL AND MIDDLE EAR.

The **external ear** proper (*pinna*) is composed of elastic fibro-cartilage, invested by a thin closely adherent skin. The skin is covered by small hairs, and connected with these are the usual sebaceous follicles. In the lobule there is a considerable amount of adipose tissue; and voluntary muscular fibres are in places attached to the cartilage of the pinna, and are seen in sections.

The **external auditory meatus** is a canal formed partly of cartilage continuous with that of the pinna, partly of bone. It is lined by a prolongation of the skin and is closed by the membrana tympani. over which the skin is prolonged as a very thin layer. Near the orifice the skin has hairs and sebaceous glands, and the meatus is also provided throughout the cartilaginous part with convoluted tubular glands of a brownish-yellow colour, which yield a waxy secretion (*ceruminous glands*). They represent modified sweat-glands. A section of one is represented in fig. 623.

The **tympanum** is lined by a mucous membrane which is continuous through the Eustachian tube with the mucous membrane of the

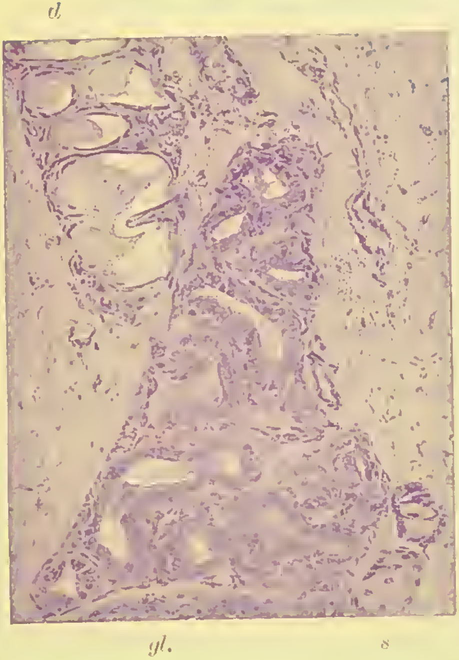

FIG. 623.—SECTION OF CERUMINOUS GLAND OF THE EXTERNAL EAR. Photograph.

d, duct of gland, having a spiral course and therefore cut several times: it is partly filled with cerumen: *gl*, secreting tubules of gland; *s*, extremity of a tubule of a sebaceous gland which extended as far as the base of the ceruminous gland.

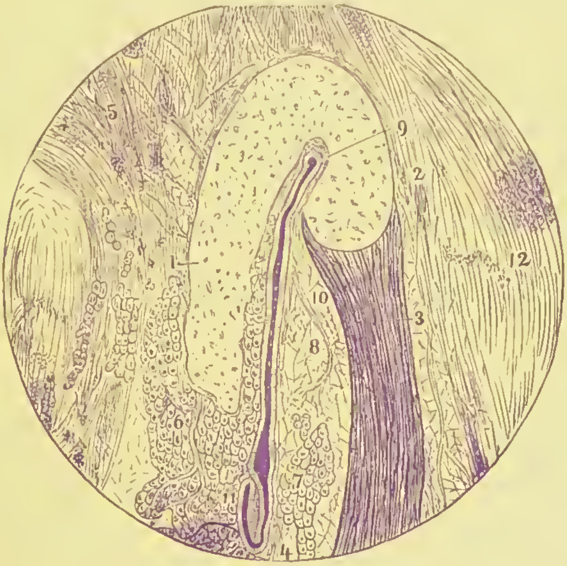

FIG. 624.—SECTION ACROSS THE CARTILAGINOUS PART OF THE EUSTACHIAN TUBE. (Rüdinger.)

1, *2*, bent cartilaginous plate; *3*, musc. dilatator tubæ; to the left of *4*, part of the attachment of the levator palati muscle; *5*, tissue uniting the tube to the base of the skull; *6* and *7*, mucous glands; *8*, *10*, fat; *9* to *11*, lumen of the tube; *12*, connective tissue on the lateral aspect of the tube.

pharynx; it is also prolonged into the mastoid cells. The epithelium is columnar and ciliated in some parts, but in others—*e.g.* roof, promontory, ossicles, and membrana tympani—it is a pavement-epithelium.

The **membrana tympani** is a thin membrane formed of fibrous bundles which radiate from a central depression (umbo). Within the radial fibres are a few annular bundles. Covering the fibrous membrane externally is a thin layer continuous with the skin of the meatus; covering it internally is another thin layer, derived from the mucous membrane of the tympanic cavity. A few blood-vessels and lymphatics are distributed to the membrane, chiefly in the cutaneous and mucous layers.

The **Eustachian tube** is the canal leading from the tympanum to the pharynx. It is formed of bone near the tympanum, but below, near the pharynx, it is bounded partly by a bent piece of cartilage (fig. 624, 1, 2), partly by fibrous tissue. The latter contains numerous mucous glands (6, 7), which open into the tube, and on the outer side a band of muscular tissue (3) which joins the tensor palati. The epithelium is ciliated.

LESSON L.

THE INTERNAL EAR.

1. Sections across one of the membranous semicircular canals of a fish (skate).

2. Longitudinal sections through the ampulla of a semicircular canal (skate).

1 and 2 may be hardened in chromic and osmic acid (see below under 5) and imbedded in celloidin.

The semicircular canals and their ampullæ may also be seen cut across in sections of the petrosal of the guinea-pig or other mammal.

3. Golgi preparations of the macula of the utricle from the skate.

4. Teased preparations of the auditory-epithelium of an ampulla or of the macula of the utricle, from the skate.

5. Vertical sections through the middle of the cochlea of a mammal (guinea-pig).

The cochlea is put quite fresh into 0·2 per cent. chromic acid containing one-fifth its volume of 1 per cent. osmic acid, or into Flemming's solution, or 10 per cent. formol. The decalcification can be effected by the use of the phloroglucin-nitric acid fluid, or by sulphurous acid.[1] When decalcified, the preparation is well washed, and then transferred to alcohols of gradually increasing strength.

In preparing sections of the above three preparations it is advisable, in order that the epithelium should be kept in position, to imbed in celloidin. If the paraffin method of imbedding be used, the sections are fixed to the slide by an adhesive process. The organ should preferably be stained in bulk.

6. Teased preparations of the epithelium of the organ of Corti from the guinea-pig.

Both 4 and 6 are made from osmic preparations.

Make sketches from all these preparations under the high power.[2]

The **labyrinth**, which is the essential part of the auditory organ, consists of a complex membranous tube lined by epithelium and filled with endolymph, contained within a bony tube—the osseous labyrinth—of corresponding complexity of shape (figs. 625, 626). The membranous labyrinth does not wholly fill the bony cavity; the rest of the space is occupied by perilymph. The membranous labyrinth (fig. 625) is composed of the *utricle* (*u*), and the three *semicircular canals* (each with an enlargement or *ampulla* which opens into it), the *saccule* (*s*), and the *canal of the cochlea* (*c.c.*).

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[1] See Appendix.

[2] For details of the somewhat complicated methods of obtaining the various parts of the labyrinth for microscopical examination, the student is referred to the author's *Course of Practical Histology*.

The branches of the auditory nerve pass to certain parts only of the membranous labyrinth, viz., the maculæ of the utricle and saccule, the cristæ of the ampullæ, and along the whole length of the canal of the cochlea (the shaded parts in fig. 625).

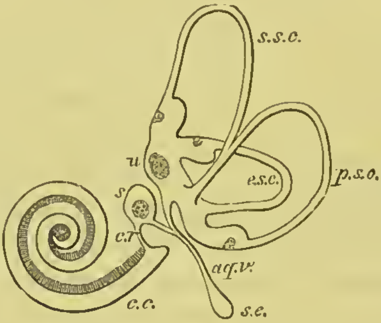

FIG. 625.—PLAN OF THE RIGHT MEMBRANOUS LABYRINTH VIEWED FROM THE MESIAL ASPECT. $\frac{2\frac{1}{2}}{1}$.

u, utricle, with its macula and *s.s.c.*, *p.s.c.*, and *e.s.c.*, the three semicircular canals with their ampullæ; *s*, saccule; *aq.v.*, aquæductus vestibuli; *s.e.*, saccus endolymphaticus; *c.r.*, canalis reuniens; *c.c.*, canal of the cochlea.

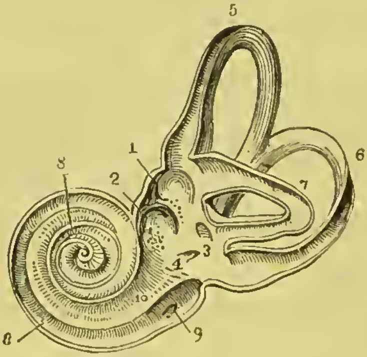

FIG. 626.—VIEW OF THE INTERIOR OF THE LEFT OSSEOUS LABYRINTH.

The bony wall of the labyrinth is removed superiorly and externally. 1, fovea hemi-elliptica; 2, fovea hemisphærica; 3, common opening of the superior and posterior semicircular canals; 4, opening of the aqueduct of the vestibule; 5, the superior, 6, the posterior, and 7, the external semicircular canals; 8, spiral tube of the cochlea; 9, scala tympani; 10, scala vestibuli.

At these places the lining epithelium is specially modified to form a sensory or nerve-epithelium; elsewhere it is a simple pavement-epithelium.

UTRICLE AND SACCULE WITH SEMICIRCULAR CANALS.

The **membranous semicircular canals** and the **utricle and saccule** are composed of fibrous tissue, which is adherent along one side to the endosteum of the bony canal; from the opposite side bands of fibrous tissue pass across the perilymph (fig. 627). Within the fibrous membrane is a thick clear tunica propria, which, in the semicircular canals, may form papilliform elevations in the interior of the tube.

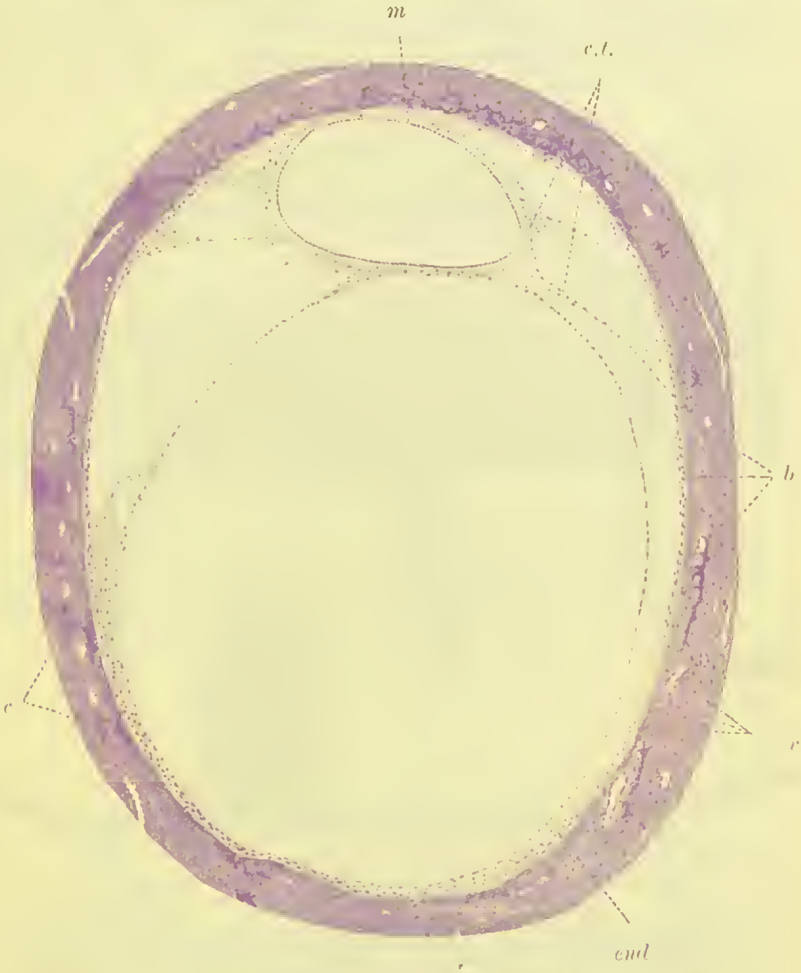

Fig. 627.—Section of a semicircular canal, new-born child. (Sobotta.) × 55.

c.t., connective-tissue strands, between membranous canal and endosteum of bony canal; *m*, membranous canal; *b*, wall of bony canal; *c*, remains of fœtal cartilage; *end*, endosteum; *v*, blood-vessels.

The places of entrance of the nerve-fibres are marked in each ampulla by a transverse, inwardly projecting ridge (*crista*), in the saccule and utricle by a thickening of the tunica propria (*macula*). The epithelium at these places is formed of columnar cells (fig. 628), which are surmounted by long, stiff, tapering hairs (*auditory hairs*, fig. 628, *h*; fig. 629). Around these *hair-cells* the axis-cylinders of the nerve-fibres ramify (fig. 630); they are therefore—like the gustatory cells of the taste-buds—sensory epithelium-cells. Between them are a number of thin and somewhat rigid nucleated cells (*fibre-cells* of Ritzius), which rest upon the basement-membrane, and are connected at their free extremity with a cuticular membrane, through which the auditory hairs project.

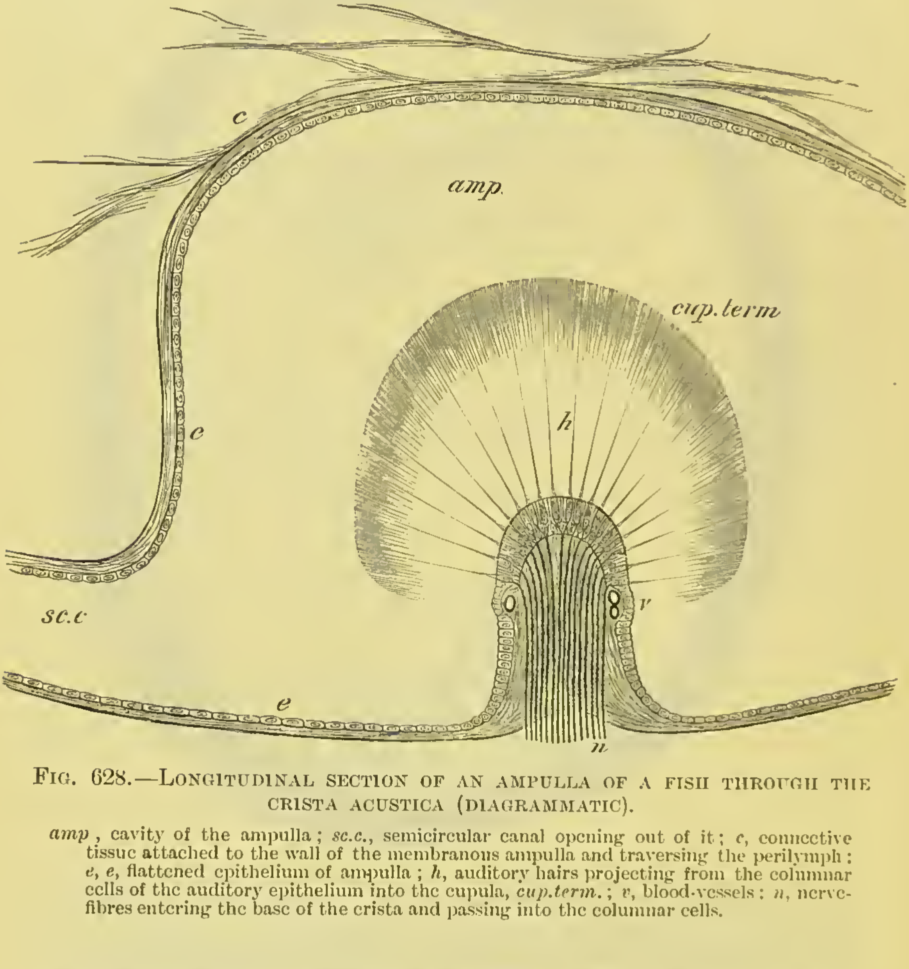

FIG. 628.—LONGITUDINAL SECTION OF AN AMPULLA OF A FISH THROUGH THE CRISTA ACUSTICA (DIAGRAMMATIC).

amp, cavity of the ampulla; *sc.c.*, semicircular canal opening out of it; *c*, connective tissue attached to the wall of the membranous ampulla and traversing the perilymph: *e*, *e*, flattened epithelium of ampulla; *h*, auditory hairs projecting from the columnar cells of the auditory epithelium into the cupula, *cup.term.*; *v*, blood-vessels: *n*, nerve-fibres entering the base of the crista and passing into the columnar cells.

The auditory hairs do not jut freely into the endolymph, but into a soft mucus-like substance, of a dome-like form in the ampullæ (*cupula terminalis*, figs. 628, 629), and which in the saccule and utricle has a mass of calcareous particles (*otoliths*) imbedded in it.

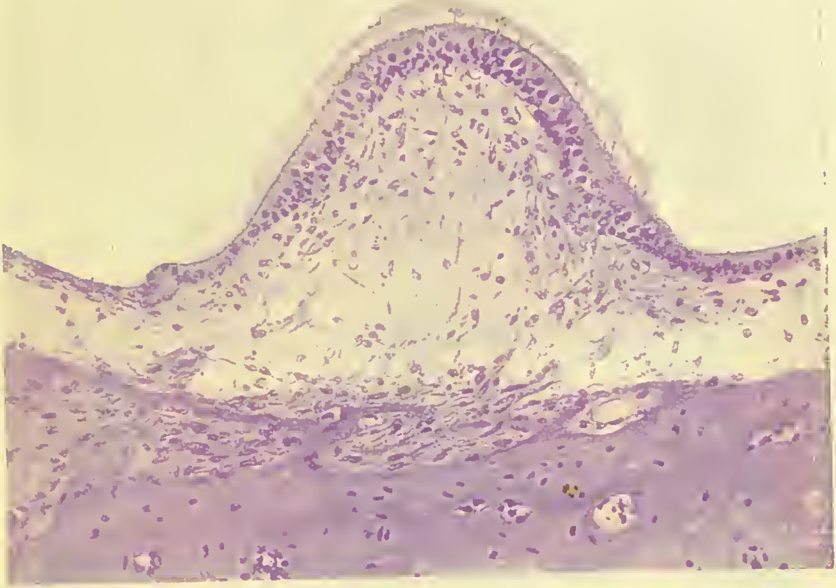

FIG. 629.—SECTION OF AMPULLA OF GUINEA-PIG. Photographed from a preparation by H. Pringle.

e, epithelium, becoming columnar over the crista, where the cells are furnished with hairlets; *c*, corium of delicate connective tissue, with the nerve-fibres passing to the epithelium; *b*, bone, with canals containing bundles of nerve-fibres.

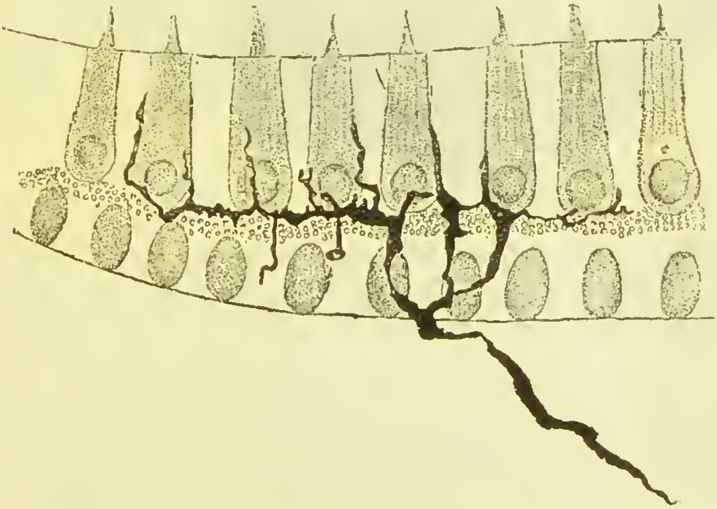

FIG. 630.—NERVE TERMINATIONS IN MACULA: GOLGI METHOD. (v. Lenhossék.)

COCHLEA.

The **cochlea** consists of a bony tube coiled spirally around an axis which is known as the *columella* (figs. 631, 632). The tube is divided longitudinally by a partition which is formed partly by a projecting lamina of bone (*spiral lamina*), partly by a flat membrane (*basilar membrane*), into two parts or *scalæ*; the upper (supposing the cochlea resting base downwards) being termed the *scala vestibuli*, the lower *scala tympani*; the latter is closed near its larger end by the membrane of the fenestra rotunda. The scalæ are lined by endosteum, and are filled with perilymph, continuous with that of the rest of the osseous

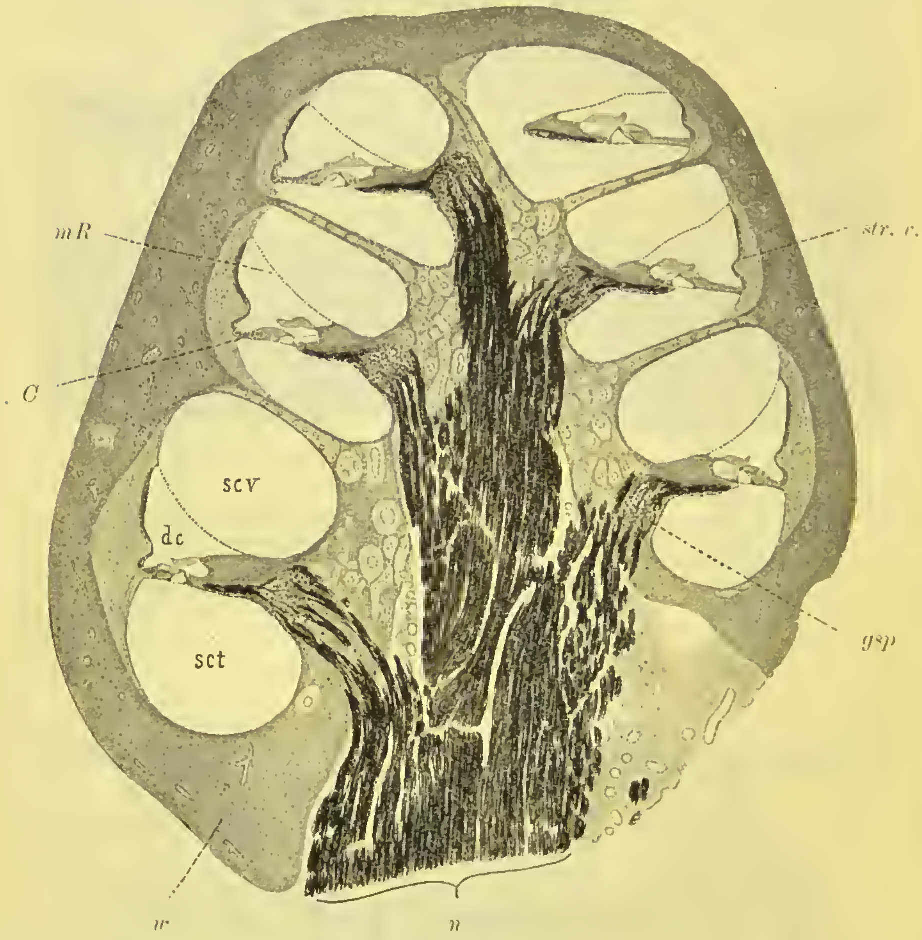

Fig. 631.—Section through the cochlea of the cat. (Sobotta.) ×25.

dc, duct of cochlea; *scv*, scala vestibuli; *sct*, scala tympani; *w*, bony wall of cochlea; *C*, organ of Corti on membrana basilaris; *mR*, membrane of Reissner; *n*, nerve-fibres of cochlear nerve; *gsp*, ganglion spirale; *str.v.*, stria vascularis.

labyrinth at the commencement of the scala vestibuli; they communicate at the apex by an opening, the *helicotrema*.

The scala vestibuli does not occupy the whole of that part of the bony tube of the cochlea which is above the partition. Its outer and lower third is cut off by a delicate connective-tissue membrane (*membrane of Reissner*, fig. 633, *R*), which springs from near the end of the spiral lamina, and passes upwards and outwards to the outer wall, thus separating a canal (*d.c.*) triangular in section, which is lined by epithelium, and represents the membranous labyrinth of the cochlea (*duct or canal of the cochlea*).

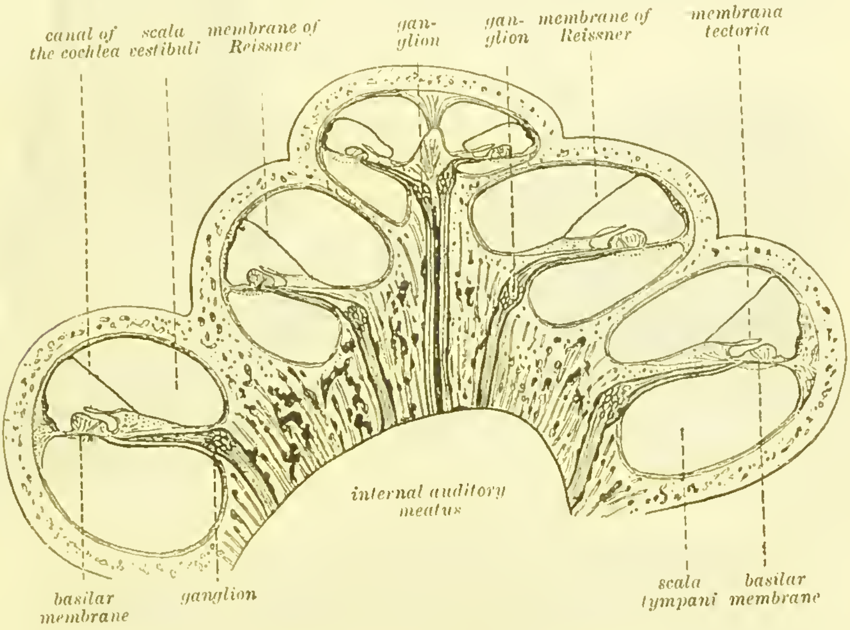

FIG. 632.—VERTICAL SECTION THROUGH THE MIDDLE OF THE HUMAN COCHLEA. Diagrammatic.

Canal of the cochlea.—The floor of the canal of the cochlea is formed (1) of the extremity of the spiral lamina, which is thickened above by a peculiar kind of connective tissue, forming an overhanging projection known as the *limbus* (fig. 633, *l*); and (2) of the basilar membrane (*b.m.*), which stretches across from the end of the bony lamina to the outer wall, and is attached to this by a projection of reticular connective tissue termed the *spiral ligament* (*l.sp*).

The *basilar membrane* is composed of stiff straight fibres, which extend from within out, and are imbedded in a homogeneous substance. The membrane is covered below by a layer of connective tissue continuous with the endosteum of the scala tympani; above the modified epithelium which forms the *organ of Corti* rests upon it. It becomes gradually broader in the upper turns of the cochlea (rather more than twice as broad in the uppermost as in the lowermost turn), and its constituent fibres become therefore gradually longer.

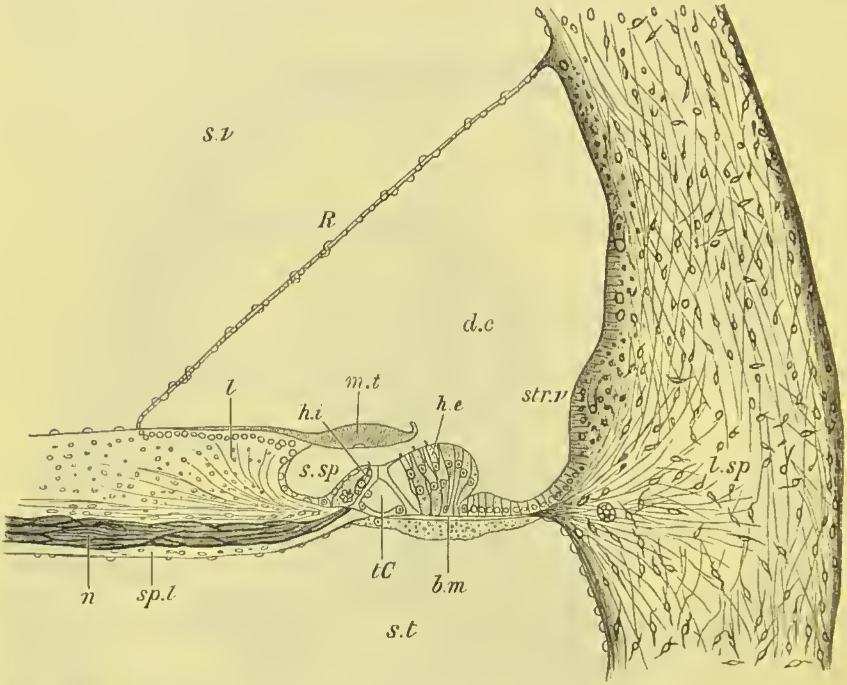

Fig. 633.—Vertical section of the first turn of the human cochlea. (G. Retzius.)

s.v, scala vestibuli; *s.t*, scala tympani; *d.c*, canal or duct of the cochlea; *sp.l*, spiral lamina; *n*, nerve-fibres; *l.sp*, spiral ligament; *str.v*, stria vascularis; *s.sp*, spiral sulcus; *R*, section of Reissner's membrane; *l*, limbus laminæ spiralis; *m.t*, membrana tectoria; *tC*, tunnel of Corti; *b.m*, basilar membrane; *h.i*, *h.e*, internal and external hair-cells.

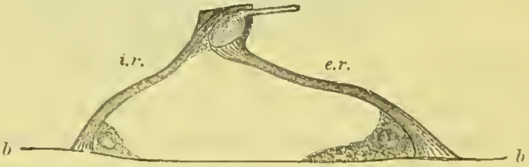

Fig. 634.—A pair of rods of Corti, from the rabbit's cochlea, in side view. Highly magnified.

b, *b*, basilar membrane; *i.r.*, inner rod; *e.r.*, outer rod. The nucleated protoplasmic masses at the feet are also shown.

The **organ of Corti** consists of the following structures:

1. The *rods of Corti*, two series (inner and outer) of stiff, striated structures, of a peculiar shape, the inner somewhat like a human ulna, the outer like a swan's head and neck (fig. 634). They rest by one

extremity (the foot) on the basilar membrane a short distance apart, and are inclined towards one another, their larger ends (heads) being jointed together; the series of rods thus inclose a sort of tunnel, the floor of which is formed by a part of the basilar membrane (fig. 636). Close to their feet may usually be seen the remains of the cells from which they have been formed. The inner rods are narrower and rather more numerous than the outer. The head of each outer rod has a process which extends outwards and is known as the phalangeal process. This forms part of—

2. A *reticular lamina* (fig. 636, *l.r.*), which is a cuticular structure extending like a wire-net over the outer epithelium-cells of the organ of Corti, and is composed of two or three series of stiff fiddle-shaped rings (*phalanges*) cemented together in such a manner as to leave square or oblong apertures through which the hair-cells (see below) project.

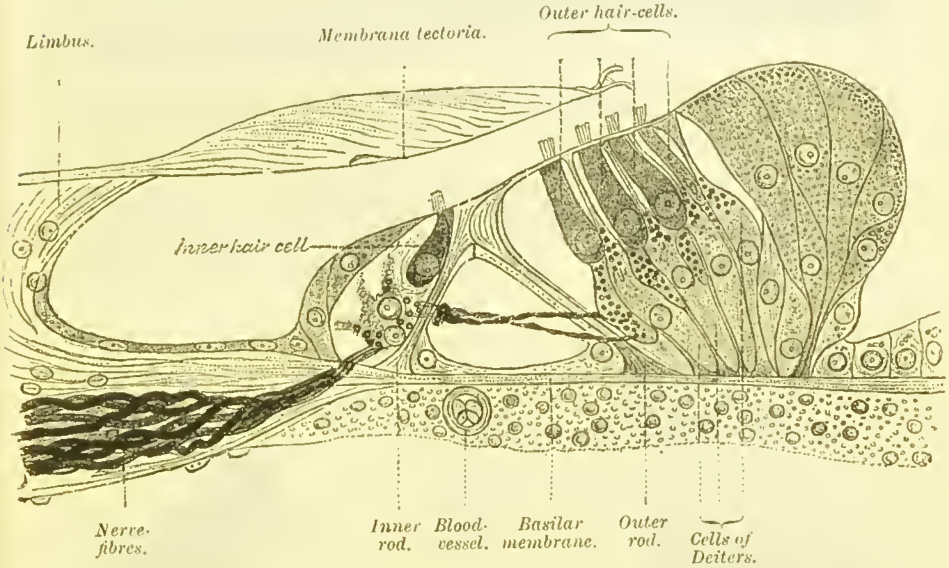

FIG. 635.—SECTION THROUGH THE ORGAN OF CORTI OF THE HUMAN COCHLEA. (G. Retzius.) Highly magnified.

3. The *outer hair-cells* placed external to the rods of Corti. These are epithelium-cells of columnar shape, arranged in three or four series (fig. 635). The free extremity of the cell is surmounted by a bundle of short *auditory hairs*, and projects through one of the apertures in the reticular lamina; the fixed extremity is prolonged into a stiff cuticular process, which is attached to the basilar membrane. Between them are other supporting cells which are tapered in the same manner, but rest by their larger end upon the basilar membrane, and are

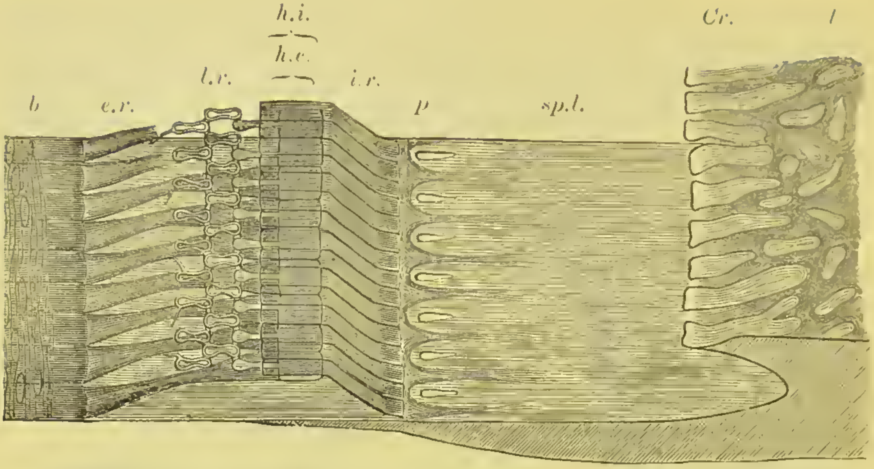

Fig. 636.—Semi-diagrammatic view of part of the basilar membrane and tunnel of Corti of the rabbit, from above and the side. Much magnified.

l, limbus; *Cr.*, extremity or crest of limbus with tooth-like projections; *b*, basilar membrane; *sp.l.*, spiral lamina with, *p*, perforations for transmission of nerve-fibres; *i.r.*, fifteen of the inner rods of Corti; *h.i.*, their flattened heads seen from above; *e.r.*, nine outer rods of Corti; *h.e.*, their heads, with the phalangeal processes extending outward from them and forming, with the two rows of phalanges, the lamina reticularis, *l.r.*

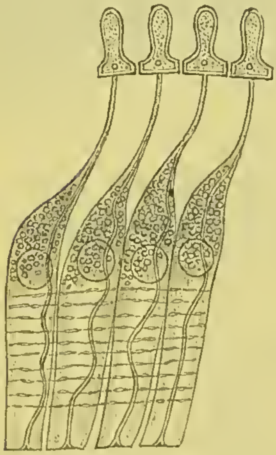

Fig. 637.

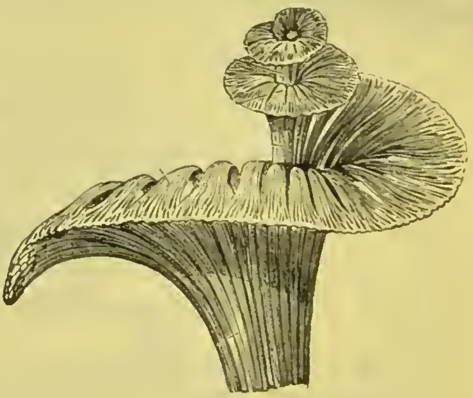

Fig. 638.

Fig. 637.—Four cells of Deiters from the rabbit. (After G. Retzius.) Highly magnified.

The varicose lines are nerve-fibrils. The phalangeal processes are attached above to a portion of the lamina reticularis.

Fig. 638.—General view of the mode of distribution of the cochlear nerve, all the other parts having been removed. (Arnold.)

prolonged above into a cuticular process which is attached to the reticular lamina (*cells of Deiters*, figs. 635, 637).

4. The *inner hair-cells* (fig. 635), placed internal to the rods of Corti. They form a single series of columnar cells surmounted by auditory hairs, lying in close apposition to the inner rods.

The remaining epithelium-cells have no important characteristics. They are long and columnar next to the outer hair-cells, but soon diminish in size, becoming cubical, and in this form they are continued over the outer wall of the cochlear canal. Here they cover a very vascular membrane (*stria vascularis*, fig. 633, *str.v.*), which is frequently pigmented; its capillary blood-vessels penetrate between the epithelium-cells. Internal to the inner hair-cells the epithelium also soon becomes cubical; it is prolonged in this form over the limbus

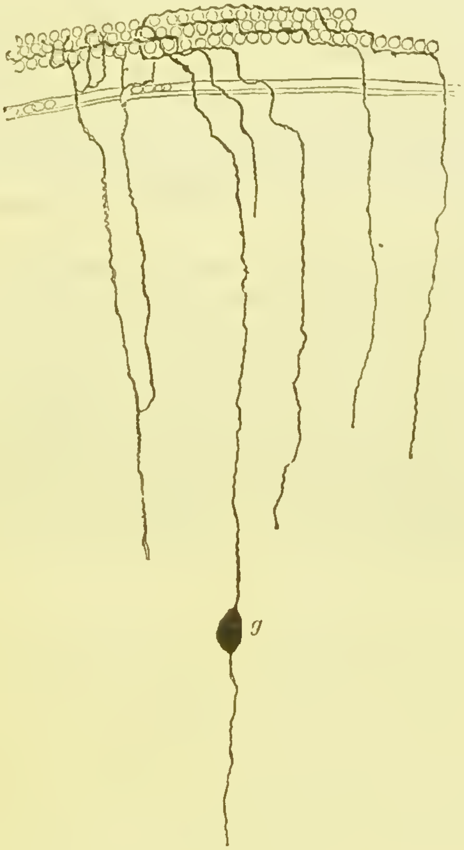

Fig. 639.—Ending of some of the fibres of the cochlear nerve amongst the hair-cells. (G. Retzius.)

This preparation is made by Golgi's method, and is viewed from above. *g*, a cell belonging to the spiral ganglion.

of the spiral lamina. The epithelium of Reissner's membrane is of the pavement variety.

The *membrana tectoria* (figs. 633, 635) is a soft, fibrillated structure, which is attached along the upper surface of the limbus where it is thin: it lies like a pad over the organ of Corti. It thins out somewhat towards the distal margin, here becoming somewhat reticular, and, according to Retzius, it is attached to the lamina reticularis. In sections it usually appears raised a short distance above the auditory hairs, but it is probable that it always rests upon them during life.

The fibres of the cochlear branch of the auditory nerve enter the base of the columella, and run in canals through its substance (figs. 631, 632), being gradually deflected outwards as they pass upwards into the spiral lamina, at the base of which they swell out into a ganglionic cord (*spiral ganglion*). The fibres take origin from the cells of this ganglion.

After traversing the spiral lamina they emerge in bundles, and the fibres then, having lost their medullary sheath, pass into the epithelium of the inner hair-cell region. Here some of them course at right angles and are directly applied to the inner hair-cells, whilst others cross the tunnel of Corti, to become applied in like manner to the outer hair-cells and the cells of Deiters (figs. 635, 639). They apparently lie between and in close contact with these cells, but there does not appear to be any direct continuity between the nerve-fibrils and the cell-substance.

APPENDIX.

Mounting solutions :—1. *Normal salt solution.*—A 0·6 to 0·9 per cent. solution of common salt is used in place of serum for mounting fresh tissues for immediate examination. The lower percentage is used for frog's tissues, the higher for mammals. Ringer's solution (see p. 30, footnote) may in many cases be substituted for normal salt solution with advantage. Preparations mounted in these solutions cannot be preserved permanently.

2. *Glycerine*, diluted with an equal quantity of water. The cover-glass may be fixed by gold size.

3. *Canada balsam*, from which the volatile oils have been driven off by heat, dissolved in xylol.

4. *Dammar varnish*, made by dissolving dammar resin in xylol. The solution is filtered through paper wetted with chloroform. This is used for the same purposes as xylol balsam and has the advantage of remaining colourless, whereas Canada balsam becomes yellow with keeping.

5. *Acetate of potassium*, a nearly saturated solution. This is the best medium for osmic preparations and for iodine-stained liver, to show glycogen within the cells. The cover-glass may be fixed by soluble glass or by gold size.

General methods of preserving and hardening tissues and organs.[1]—The following fluids may be used: Alcohol (75 per cent. to absolute); acetone; Carnoy's fluid (absolute alcohol 60 c.c., chloroform 30 c.c., glacial acetic acid 10 c.c.); formol (diluted with from 9 to 99 parts of water); corrosive sublimate (saturated solution); chromic acid solution (1 in 200 to 1 in 500, to which glacial acetic acid may advantageously be added in the proportion of 2 parts acetic acid to 1000 chromic solution); picric acid solution (saturated, either alone or containing 2 parts of nitric or sulphuric acid to 1000); Mann's fluid (a mixture of equal parts of saturated aqueous solutions of mercuric chloride and picric acid); osmic acid solution (1 per cent.); bichromate of potassium solution (3 per cent.), to which for more rapid hardening glacial acetic acid may be added to the extent of 5 per cent. or less; Müller's fluid (bichromate of potash 2½ parts, sulphate of soda 1 part, water 100 parts); Zenker's fluid (which is Müller's fluid containing 5 parts per cent. of mercuric chloride, to which 5 c.c. of acetic acid is added at the time of using); and mixtures of Müller's fluid and osmic acid 1 per cent. in varying proportions.

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[1] Details of the methods of preparing fixing and staining solutions, as well as a discussion of the theory of their action, will be found in Mann's *Physiological Histology*, Oxford, 1902.

It is best, if possible, to inject the fluid used for hardening into the blood-vessels after washing them out with warm normal saline; if this is not possible, very small pieces of tissue should be taken, and always a considerable amount of the hardening fluid.

The fluid of most general application is formol. This is a 40 per cent. solution of formaldehyde. Mixed in the proportion of 10 parts formol to 90 water, it penetrates readily and hardens quickly. The tissue may remain in formol a few days and should then be transferred to alcohol. For rapid fixation a very small piece of the tissue is placed in 10 per cent. formol and warmed to a temperature of about 40° or 50°; it will be sufficiently hardened in half an hour, and may then be transferred first to weak and then gradually to absolute alcohol, so that it is ready for the preparation of sections in about an hour.

Pure acetone is also of utility for rapid fixation and hardening. Small pieces of the tissue are dropped into a large amount of acetone, which not only fixes and hardens but also dehydrates, so that the tissue can be transferred in an hour or so direct to molten paraffin for embedding. But much better results are got by placing in 10 per cent. formol for thirty minutes before transferring to acetone.

For preserving the structure of cells and nuclei, one of the best fixing fluids is that recommended by Flemming. This consists of 15 vols. of 1 per cent. chromic acid, 4 vols. of 2 per cent. osmic acid, and 1 vol. glacial acetic acid. It must be freshly prepared. It is sometimes diluted with from two to five times its bulk of water before use. One or two days is sufficient for fixation and hardening. The tissue should be washed for several hours in running water after removal from the mixture, and then placed in dilute alcohol. Tissues fixed in any mixture containing osmic acid stain with difficulty. The best stains for use in this case are saffranin, gentian violet, or carmalum. Carnoy's fluid (see previous page) is in many cases excellent for cell-structure and mitotic changes, and very rapid in its action.

Tissues to be hardened in alcohol are usually placed at once in absolute alcohol, but for some tissues it is best to begin with 50 per cent. alcohol, and pass the pieces through successive grades of 75 per cent., 95 per cent., into absolute alcohol, leaving them a few hours in each. They are ready for cutting as soon as they are dehydrated, but as a rule they may be left a long time in alcohol without deterioration. Organs which contain much fibrous tissue, such as the skin and tendons, should not go into stronger alcohol than about 80 or 90 per cent.; otherwise they become too hard to cut. Alcohol is generally used after the other fixing reagents, partly to complete the hardening, partly on account of its dehydrating property, since previous to embedding in paraffin all trace of water must be eliminated from the tissue. If mercuric chloride be used for hardening, tincture of iodine must be added to the alcohols subsequently used (except the final alcohol), to get rid of the excess of sublimate. Mercuric chloride in alcohol (saturated solution) is one of the most rapid fixing and hardening reagents, and may be used if sections are desired within a very short time. It can also be used in place of alcohol and ether mixture for fixing blood films (Lesson II., § 5), in which case it may be saturated with eosin, and used for fixing and staining at the same time. An immersion of 5 minutes is sufficient.

Many tissues can be instantly hardened by being plunged for a minute into boiling water and then placed in alcohol: this is not, however, a good method for glandular organs.

For tissues that are to be hardened in chromic acid an immersion of from seven to fourteen days is generally necessary; they may then, after washing for some hours or days in tap-water, be placed in alcohol for preservation and to complete the process of hardening. The alcohol should be changed once or twice.

Organs placed in bichromate of potassium or Müller's fluid are ready for section in a fortnight or three weeks; they may, however, be left for a much longer time in those fluids without deterioration.

With picric acid the hardening process is generally complete in two or three days; the organs may then be transferred to alcohol, which ought to be frequently changed.

The hardening of the brain and spinal cord in Müller's fluid takes from three weeks to as many months. It can be hastened by warmth, and by the addition of acetic acid, or by placing small pieces in Marchi's solution (see below), after they have been a week or ten days in Müller's fluid.

Tissues containing calcareous matter, *e.g.* bone and tooth, may be rapidly decalcified in a solution made by dissolving, with the aid of heat, 1 grm. phloroglucin in 10 c.c. nitric acid, and filling up to 100 c.c. with water, to which more nitric acid may be added if desired. Another rapid decalcifying fluid is commercial sulphurous acid solution. If it is desired to preserve the soft parts within the bone, it should first be placed for a few hours in 10 per cent. formol. For decalcifying more slowly a 1 to 5 per cent. solution of nitric acid in water or alcohol, a saturated solution of picric acid containing a superabundance of crystals, or a 1 per cent. solution of chromic acid are employed.

Embedding of hardened tissues, and preparation of sections.—Sections are most advantageously made with some form of microtome. It is generally needful to support the hardened tissue whilst it is being cut, and with this object it is embedded in some substance which is applied to it in the fluid condition and becomes solid on standing. The embedding substance can either simply inclose the tissue, or the tissue may be soaked in it; the latter method is the one commonly employed.

The embedding substance chiefly used is paraffin of about 50° C. melting point. The precise temperature depends upon that of the atmosphere. In summer a paraffin of higher melting point may be required.

Embedding in paraffin.—Before being soaked in melted paraffin, the piece of tissue may be stained in bulk (see p. 553); it is then dehydrated by a series of alcohols (50 per cent., 75 per cent., 95 per cent.), finishing up with absolute alcohol; after which it is soaked in cedar-wood oil, xylol, or chloroform. It is now transferred to molten paraffin, which should not be too hot, and is soaked in this for one or several hours, according to thickness. Very delicate objects are sometimes passed through a solution of paraffin in chloroform. When thoroughly impregnated with the paraffin the object is placed in a mould or glass which has been smeared with glycerine, and is covered with molten paraffin which is allowed to cool quickly. A square block of the paraffin containing the tissue is then fixed in the desired position on the microtome, thin sections are cut and fixed to a slide (see below), the paraffin dissolved out by turpentine or xylol, and the sections mounted in Canada balsam or dammar.

If it be desired to cut a riband of successive sections, and the paraffin used prove too hard for them to stick to one another at the edges, a paraffin of lower melting point (40° C.) is smeared over the opposite sides of the block; the sections then adhere together as they are cut.

Preparation of frozen sections.—The bichromatic solutions and formol are the best fluids to use for preserving tissues which are to be frozen in place of being embedded. Any alcohol employed for fixation should be thoroughly washed out with water. The tissue is soaked in gum-water before being placed upon the freezing microtome. A thin syrup of either gum arabic or dextrin may be used.

Embedding in celloidin.—The piece to be embedded is dehydrated by alcohol, and is then placed over night in a solution of celloidin in alcohol and ether similar to ordinary collodion, and afterwards in collodion of double strength. After twenty-four hours more it is removed from the celloidin (collodion) and placed upon a wood or metal holder. When the celloidin is set by evaporation of its ether the holder is plunged in alcohol (85 per cent.); after a few hours sections may be cut with a knife wetted with spirit of the same strength. The sections are placed in 95 per cent. alcohol; then passed through cedar-wood oil or bergamot oil into xylol balsam. They must not go into clove-oil, nor into absolute alcohol. The advantage of the method is that the celloidin, which is quite transparent, need not be got rid of in mounting the sections, and serves to keep the parts of a section together; it is thus very useful for friable tissues or for large sections. The tissue may either be stained in bulk before embedding, or the sections may be stained.

Microtomes.—A section-cutting apparatus or microtome is essential for histological work. Useful instruments for students are the Cathcart microtome for freezing and the tripod microtome for objects which have been embedded in paraffin.

The tripod microtome is a simple and efficient little instrument, and has the advantage of being inexpensive. It consists of a metal frame (fig. 640) in which the razor is fixed, provided with a micrometer screw by which the height of the razor-edge is adjusted. The paraffin block containing the tissue is fixed by the aid of heat on a flat piece of glass over which the tripod slides. The razor-edge is lowered after each successive section.

In the Cathcart freezing microtome (fig. 641) the tissue, after being soaked in gum-water, is placed on a metal plate and frozen by playing an etherspray on the under surface of the plate. The plate is moved upwards by a finely-cut screw, and the knife or plane used to cut the sections is guided over the plate by passing over glass slips. In the Williams microtome the freezing agent is ice and salt mixture. In using any freezing microtome,

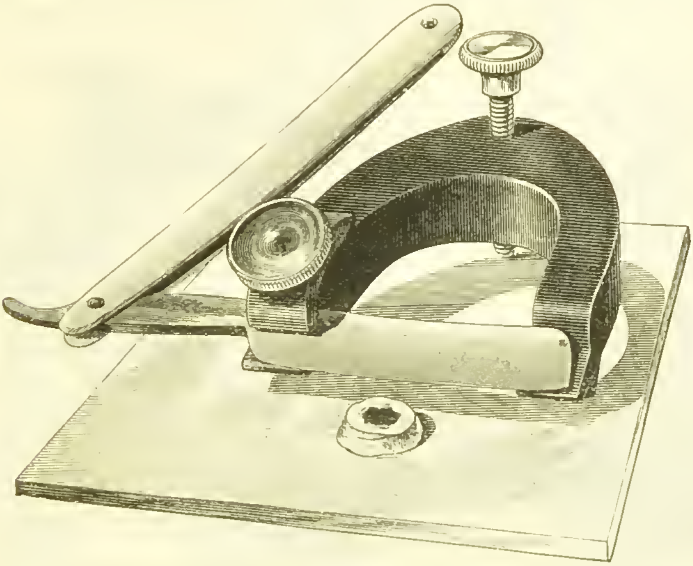

FIG. 640.—TRIPOD MICROTOME. (Birch's pattern.)

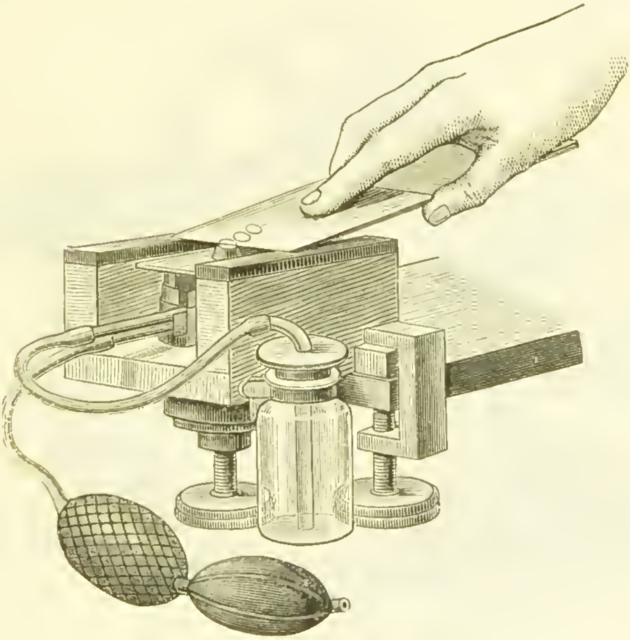

FIG. 641.—CATHCART FREEZING MICROTOME.

especially for the nervous system, it is important not to freeze the tissue too hard, or the section will roll up.

Somewhat more expensive and complicated, but also more efficient, instruments are the rocking microtome of the Cambridge Scientific Instrument Company (fig. 642) and the microtomes designed by C. S. Minot and by

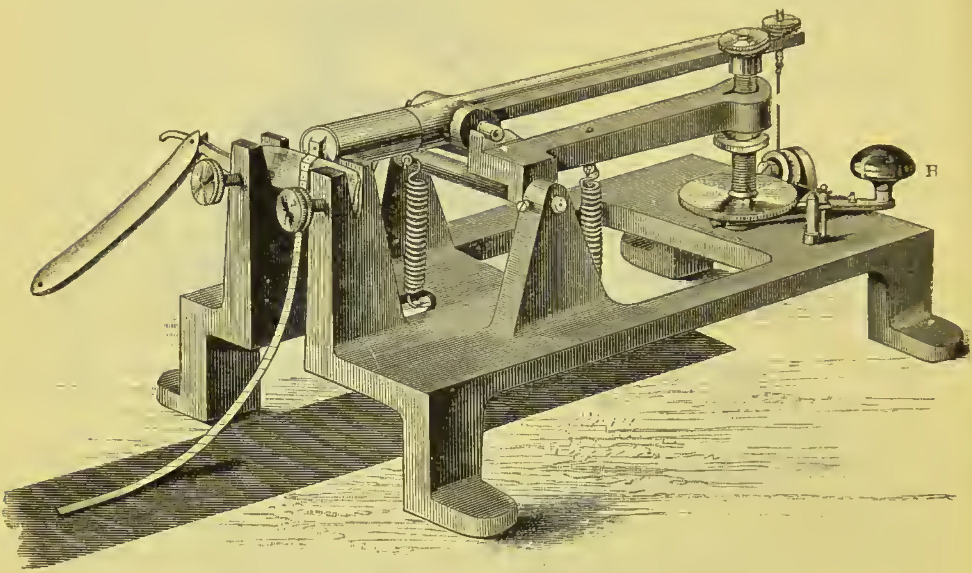

FIG. 642.—ROCKING MICROTOME.

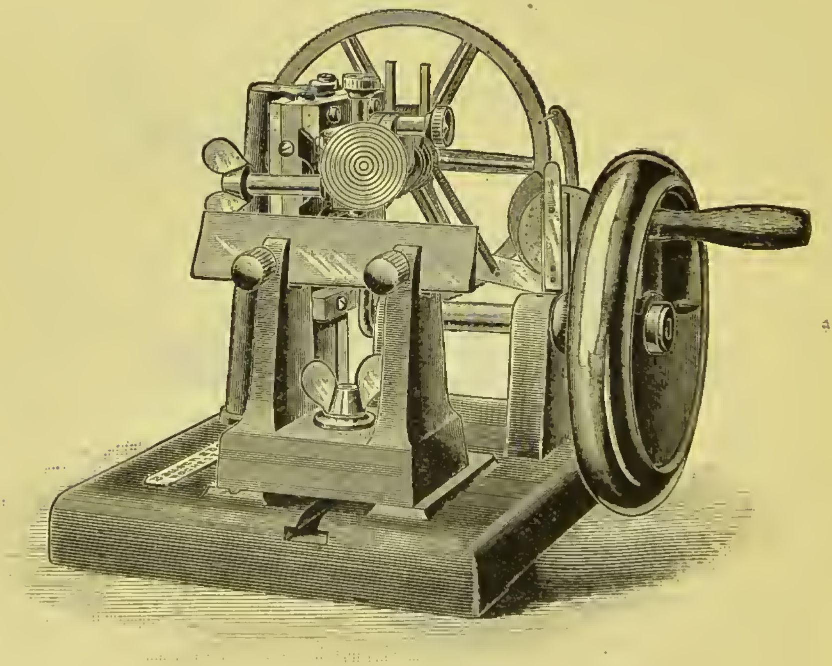

FIG. 643.—MINOT'S AUTOMATIC ROTARY MICROTOME.

Delépine. The action of all of these is automatic. For example, with the rocker microtome every to-and-fro movement of the handle, H, not only cuts a section of the tissue of definite thickness, but also moves the paraffin block forwards in readiness for the next section. And by employing a rectangular block of paraffin of the proper consistency, a long series of sections of the same object, of equal thickness, can be obtained and made to adhere together in a riband (as shown in fig. 642). The sections can be kept in series upon the slide by the employment of some adhesive method of mounting the riband.

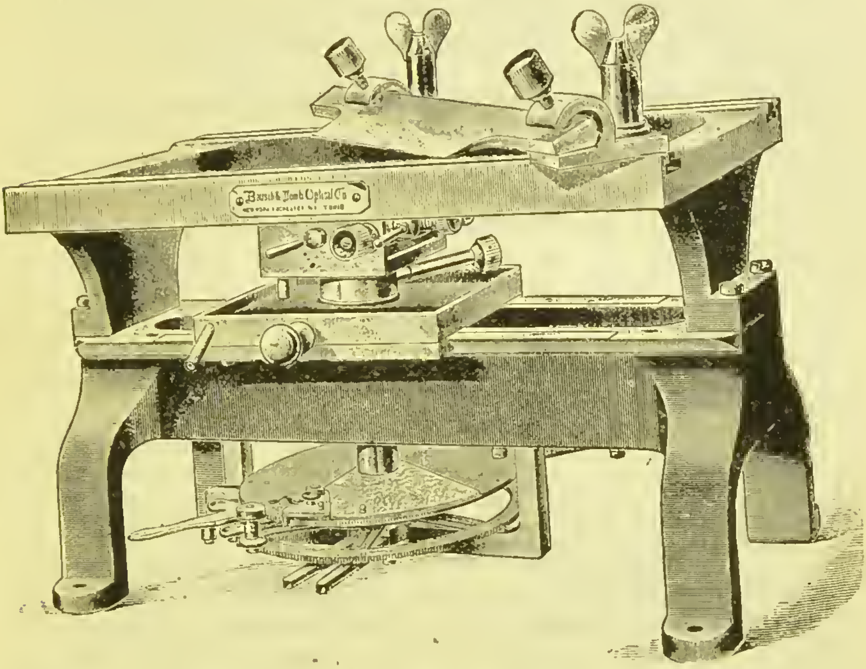
Bausch & Lomb Optical Co.

FIG. 644.—MINOT'S PRECISION MICROTOME.
This is especially adapted for large sections.

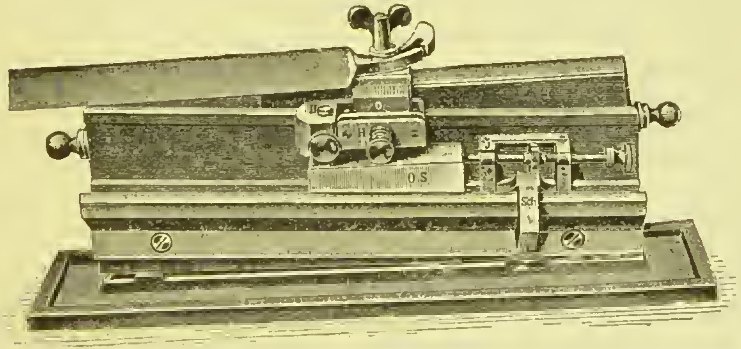

FIG. 645.—INCLINED PLANE MICROTOME.

For celloidin-embedded preparations it is necessary to cut the sections with a knife kept wetted with spirit. For this purpose a sliding microtome (figs. 644, 645), in which the knife or razor is moved horizontally over the tissue, with the edge obliquely inclined to the direction of movement is the most useful. The best arrangement for this purpose, especially for large sections of brain, is one in which the celloidin-soaked object is immersed in spirit during the actual process of making the sections. It is all-important for every kind of microtome that the knife should be in perfect order.

Methods of mounting in xylol balsam or dammar.—Individual paraffin-cut sections or ribands of sections, such as are cut with the rocking and other microtomes, are fixed to a slide or cover-glass—as a preliminary to being treated with stains and other fluids—in the following way: The slide (or cover-glass), after having been carefully cleaned, is smeared very thinly with fresh white of egg: this can be done with the finger or with a clean rag, and the slides may be put aside to dry, protected from dust. It is convenient to prepare a large number of slides at a time in this way, and to keep them at hand in a suitable receptacle. When required for use a little water is poured on to the slide and the riband of sections is placed on the water, which is then warmed on a hot plate or over a small flame until the paraffin becomes flattened out, without actually melting. The water is then drained off, the slide put in a warm place for the remainder of the water to evaporate (this will take from half an hour to an hour according to the size of the section and the temperature at which it is kept), and then heated sufficiently to melt the paraffin. It is next immersed in xylol to remove the paraffin, after which the sections may, if already stained, be mounted at once in xylol balsam or dammar; if not stained, treat, after xylol, first with absolute and then with gradually lower grades of alcohol, then water, and then stain, and finally pass through water, alcohol (in grades), clove-oil, and xylol, into xylol balsam or dammar. For many sections some of the grades of alcohol can be omitted, but it is always best to place in 50 per cent. between water and absolute alcohol.

A simpler method, but one which, in most cases, answers the purpose perfectly well, is to place the riband or the individual sections cut from paraffin on the surface of water in a basin, just sufficiently warm to flatten out the paraffin, but not to melt it, then pass a perfectly clean slide under the surface of the water and float the sections on to it; remove, drain off the water, and put the slide and sections aside for an hour or more until all the water has evaporated. The sections are found to have adhered firmly to the slide (they may, if desired, be yet more firmly fixed by drawing a brush moistened with solution of celloidin in oil of cloves over them). The paraffin can now be removed by washing the slide with xylol or immersing it in xylol. If not previously stained they can then be passed through alcohols and stained and mounted as just described. It is convenient to keep the several solutions which are required in cylindrical tubes or grooved glass receptacles in a regular row upon the working table and transfer the slide from one to the other in succession. Thus such a series would be (1) xylol; (2) absolute alcohol; (3) 75 per cent. alcohol; (4) 50 per cent. alcohol; (5) distilled water; (6) staining solution; (7) tap water; (8) distilled water; (9) 50 per cent. alcohol; (10) 75 per cent. alcohol; (11) absolute alcohol; (12) clove oil or xylol. The changes can also be effected by pouring the solutions over the sections and draining off.

The following table shows the methods which may be adopted for the treatment of paraffin-cut sections or ribands of sections:

1. Place on a slide or cover-glass in a drop of tap-water: the glass may previously have been smeared with egg-white: warm gently.
2. Drain off water and allow to dry *completely*.
3. Warm until paraffin is just melted.
4. Dissolve paraffin away with xylol.

If tissue is already stained in bulk.	If tissue is not already stained.
Mount in xylol balsam or dammar.	5. Absolute alcohol.
	6. Descending grades of alcohol.
	7. Stain
	8. Water.
	9. Ascending grades of alcohol.
	10. Xylol or bergamot oil or creosote or clove-oil.
	Mount in xylol balsam or dammar.

For sections cut by the *freezing* or *celloidin methods*, if the tissue has already been stained in bulk, the sections need only be put through the ascending grades of alcohol and bergamot oil, and then mounted in dammar. If the tissue has not already been stained, begin at No. 7.

Staining solutions.—The fluids most commonly employed for the staining of sections are: (1) Solutions of hæmatoxylin and alum; (2) solutions of carmine with or without alum; (3) certain aniline dyes. The time of immersion in the staining fluid varies according to the strength of the fluid and the mode by which the tissue has been hardened. The necessity of staining sections may be avoided if the tissue is stained in bulk before embedding. For this purpose a small piece of hardened tissue is placed for twenty-four hours or more in a moderately diluted solution of hæmalum (Milroy); this may be followed by 2 or 3 hours in a 1 per cent. solution of eosin (or erythrosin). The tissue is then passed through alcohol, which removes excess of eosin. It may be cut into sections by the paraffin or freezing methods. If the latter be employed the sections are thoroughly washed with tap-water, dehydrated by alcohol, and passed through clove-oil or xylol into xylol balsam or dammar. For some purposes (*e.g.* the study of ossifying cartilage) a strong alcoholic solution of magenta is useful for staining in bulk; from this the tissue goes direct into oil of cloves, and after being soaked with this it is passed through xylol into molten paraffin. Sections may also be stained whilst still infiltrated with paraffin by floating them on to the surface of the staining solution, which is gently warmed (but not enough to melt the paraffin). They generally require far longer exposure to the stain. The subsequent treatment is quite simple, for they need only be transferred to warm water, floated on to a slide and allowed to dry. The paraffin is then melted, dissolved away with xylol, and the sections are mounted in dammar.

The following are some of the principal staining solutions and methods of staining for special purposes :

1. *Delafield's hæmatoxylin.*—To 150 cubic centimetres of a saturated solution of potash alum in water add 4 cubic centimetres of a saturated solution of hæmatoxylin in alcohol. Let the mixture stand eight days, then decant, and add 25 cubic centimetres of glycerine and 25 cubic centimetres of methylic alcohol. The solution must stand a few days before it is ready for use.

To stain sections add a few drops of this solution to a watch-glassful of *distilled* water. If overstained the excess of colour can be removed by alcohol containing 1 per cent. nitric or hydrochloric acid. With long keeping this solution becomes red instead of blue ; a trace of ammonia will restore the blue colour.

2. *Ehrlich's hæmatoxylin.*—Dissolve 2 grammes hæmatoxylin (or, better, hæmateïn) in 100 cubic centimetres alcohol ; add 100 cubic centimetres water, 100 cubic centimetres glycerine, and 10 cubic centimetres glacial acetic acid : add potash alum to saturation. This solution will keep almost indefinitely : it is valuable for staining in bulk, as it does not easily overstain. For staining sections it is best to dilute the solution either with distilled water or with 30 per cent. alcohol. After the sections have been stained they must be thoroughly washed with tap-water. This develops the blue colour of the hæmatoxylin.

3. *Kultschitzky's hæmatoxylin.*—Dissolve 1 gramme hæmatoxylin in a little alcohol, and add to it 100 cubic centimetres of a 2 per cent. solution of acetic acid. This solution is valuable for staining sections of the nervous system (see Weigert-Pal process).

4. *Hæmalum.*—Hæmatoxylin - alum solutions acquire their colouring properties only as the hæmatoxylin on keeping becomes converted into hæmateïn. The latter substance may, therefore, as recommended by Mayer, be used advantageously in place of hæmatoxylin if the stain is required immediately. The following mode of preparing the solution may be adopted : Dissolve 50 grammes of ammonia alum in 1 litre of water, and 1 gramme of hæmateïn in 100 c.c. of rectified spirit. Add the hæmateïn solution gradually to the alum. The mixture is ready for staining at once, either as it is or diluted with distilled water. A small piece of thymol or a little carbolic acid should be added to prevent the growth of moulds.

5. *R. Heidenhain's method.*—After hardening in alcohol, or in saturated solution of picric acid and then in alcohol, place the tissue from twelve to fourteen hours in a $\frac{1}{3}$ per cent. watery solution of hæmatoxylin, and then from twelve to twenty-four hours more in a $\frac{1}{2}$ per cent. solution of yellow chromate of potash, which may be changed more than once. Then wash in water, place in alcohol, pass through xylol, and embed in paraffin.

6. *M. Heidenhain's method.*—Harden in sublimate, followed by alcohol : fix sections to slide by water method ; treat with iodised alcohol, transfer to

2·5 per cent. iron-alum (solution of sulphate (or tartrate) of iron and ammonia) and leave a quarter of an hour or longer; rinse with distilled water; place in 1 to 0·5 per cent. pure hæmatoxylin in water containing 10 per cent. alcohol for a few minutes; wash with water; differentiate in the iron and ammonia solution until nearly decolorised; wash for fifteen minutes in tap-water; dehydrate and mount in the usual way. This method is especially adapted for exhibiting the centrosomes of cells. It is also a good general method for most tissues.

Both the process of mordanting with iron-alum and the subsequent staining with hæmatoxylin may be considerably prolonged with advantage for some tissues.

7. *Carmalum* (Mayer).—Useful either for sections or bulk-staining. If the sections are subsequently passed through alcohol containing picric acid in solution a double stain is produced.

Carminic acid - - - - -	1 gramme.
Ammonia alum - - - - -	10 grammes.
Distilled water - - - - -	200 c.c.

Boil together, allow to cool, and filter. Add thymol or a little carbolic acid to prevent the growth of moulds.

8. *Carminate of ammonia.*—Prepared by dissolving carmine in ammonia, and allowing the excess of ammonia to escape by slow evaporation. The salt should be allowed to dry and be dissolved in water as required.

9. *Picric acid.*—A saturated solution of picric acid in spirit may be used as a second stain after hæmatoxylin or carmine. Any excess of picric acid is dissolved out by rinsing with strong spirit. This form of double stain is valuable for exhibiting keratinised tissues and muscle-fibres.

10. *Van Gieson's stain.*—This, which is a saturated solution of picric acid in water, with 5 c.c. of a 1 per cent. water solution of acid fuchsin added to each 100 c.c., stains connective-tissue fibres bright red; muscle fibres and epithelium yellow. The sections may first be stained deeply with hæmalum; then placed in Van Gieson's stain for some minutes; then passed through 75 per cent. alcohol, absolute alcohol and clove oil or xylol, and mounted in dammar. The method is very suitable for frozen and celloidin sections.

11. *Picro-carminate of ammonia*, a double stain. α. *Ranvier's picro-carmine.*—To a saturated solution of picric acid add a strong solution of carmine in ammonia, until a precipitate begins to form. Evaporate on the water bath (or, better, allow it to evaporate spontaneously) to one half its bulk; add a little carbolic acid to prevent the growth of moulds; filter from the sediment.

β. *Bourne's picro-carmine.*—"Add 5 c.c. of ammonia to 2 grammes carmine in a bottle capable of containing about 250 c.c. Stopper, shake, and put aside till next day. Add slowly, shaking the while, 200 c.c. of a saturated solution of picric acid in distilled water. Put aside till next day. Add slowly, constantly stirring, 11 c.c. of 5 per cent. acetic acid. Put aside till next day. Filter; to the filtrate add four drops of ammonia, put back in the stoppered bottle" (Langley).

12. *Borax-carmine.*—Dissolve 4 grammes borax and 3 grammes carmine in 100 cubic centimetres of warm water. After three days add 100 cubic centimetres of 70 per cent. alcohol, let stand two days and filter. This solution improves on keeping. It is useful for staining in bulk.

After staining with borax-carmine, the tissue should be placed in 70 per cent. alcohol containing 5 drops of hydrochloric acid to 100 cubic centimetres.

13. *Aniline dyes.*—These are used either in aqueous solution (which may contain 0·01 per cent. of caustic potash) or in water shaken up with aniline oil, and it is usual to overstain a tissue with them, and subsequently to decolorise with absolute alcohol containing $\frac{1}{5}$ its bulk of aniline oil (from which the sections can pass directly into xylol) or with acid-alcohol (1 to 10 per 1000 hydrochloric acid) followed by absolute alcohol and this by xylol. Those most employed are the "basic" dyes—methyl blue, methylene blue, gentian violet, toluidin blue, thionin, saffranin, and vesuvin; and the "acid" dyes—eosin, erythrosin, acid magenta or acid fuchsin, and orange G. A double stain is obtained by combining eosin with methylene blue or toluidin blue, the sections being first stained for ten minutes in 1 per cent. aqueous eosin and then, after rinsing with water, for twenty minutes in 1 per cent. of the blue solution, after which they are decolorised by absolute alcohol or absolute alcohol and aniline oil. The decolorisation is arrested by xylol. Other good double stains are the eosin-methyl blue mixture devised by G. Mann;[1] and Jenner's stain, which is made by dissolving in pure methyl alcohol the precipitate which is produced when eosin solution is added to methylene-blue solution. Jenner's stain is valuable for blood films. For the same purpose Ehrlich's triple stain is also used. This is formed by mixing together aqueous solution of orange G., acid-fuchsin, and methyl green in certain proportions.[2]

14. *Eosin.*—A 1 per cent. solution in water may be used. The sections are first stained deeply with hæmatoxylin and rinsed with water. They are then stained with the eosin solution, passed through 75 per cent. alcohol, and then through strong spirit—which is allowed to dissolve out some but not all of the eosin stain—into clove-oil: they are finally mounted in xylol balsam or dammar. Erythrosin may be used in place of eosin.

Eosin stains hæmoglobin of an orange red colour; so that the blood corpuscles are well shown when a fixing fluid has been employed which does not remove the hæmoglobin from them (such as mercuric chloride, bichromate of potassium, and formol).

15. *Muir's method of double-staining with eosin and methylene blue.*—For staining hæmoglobin and oxyphil granules in cells the method devised by Richard Muir will be found valuable. It consists in staining the sections of formol-hardened tissue (which are fixed on a slide) with saturated solution of alcohol-soluble eosin crystals dissolved in rectified spirit. This solution is poured over the sections, and evaporated over a flame until most of the alcohol is driven off. Rinse with water, place in saturated solution of potash alum for three minutes, and wash again. Decolorise with alcohol rendered

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[1] *Methods of Physiological Histology*, p. 216.

[2] It is best to purchase this solution ready-made.

very faintly alkaline with ammonia. Wash. Stain with saturated water-solution of methylene blue; wash with water; dehydrate and mount in the usual way.

16. *Acid fuchsin or magenta.*—A 1 per cent. solution in 50 per cent. alcohol (to which 1 drop of 1 per cent. alcohol-solution of gentian violet may be added per cubic centimetre) is an excellent stain for connective tissue. It may also advantageously be used for developing bone and tooth and for lymph-glands. The piece of tissue is left for several days in a 1 per cent. solution in 95 per cent. alcohol, and is then placed direct in a small quantity of clove-oil for a few hours, after which it is transferred through xylol to molten paraffin.

17. *Mallory's stain for connective tissue.*—The sections are placed for three minutes in acid fuchsin (1 per 1000); then washed in water and immersed for several minutes in phospho-molybdic acid. Wash again thoroughly in water, and place for two minutes or more in the following solution:

Aniline blue, - - - - - -	0·5 g.
Orange G., - - - - - -	2·0 g.
Oxalic acid, - - - - - -	2·0 g.
Water, - - - - - - -	100 c.c.

After being stained with this they are passed through water, alcohol, and xylol into balsam or dammar.

18. *Orcein.*—Dissolve 1 gramme orcein in 100 c.c. absolute alcohol, containing 1 c.c. hydrochloric acid. Place the sections in some of this solution in a watch-glass and warm slightly, allowing the fluid to nearly evaporate to dryness. Dehydrate in alcohol, which removes the excess of stain; pass through xylol into dammar. Orcein stains especially the elastic fibres.

19. *Flemming's method for karyokinetic nuclei.*—This is especially valuable for staining cell-nuclei in mitosis. The tissue having been appropriately fixed, small shreds or thin sections are placed for two days in saturated alcoholic solution of saffranin, mixed with an equal amount of aniline-water. They are then washed with distilled water and decolorised in aniline-alcohol or in alcohol containing 1 per 1000 hydrochloric acid until the colour is washed out from everything except the nuclei. They are then again rinsed in water and placed in saturated aqueous solution of gentian violet for two hours, washed again in distilled water, decolorised with aniline alcohol until only the nuclei are left stained, then transferred to bergamot oil or xylol, and from this are mounted in xylol balsam or dammar. Gentian violet and several other basic aniline colours may be employed in place of saffranin from the first. Delafield's hæmatoxylin (followed by acid), and Ehrlich's hæmatoxylin also stain the mitotic figures well.

20. *Staining with nitrate of silver* (Recklinghausen).—Wash the fresh tissue with distilled water; immerse in ½ to 1 per cent. nitrate of silver solution for from one to five minutes; rinse with distilled water and expose until just brown to bright sunlight either in water, 70 per cent. alcohol, or glycerine and water. The tissue, which is generally a thin membrane, may either be mounted in glycerine or it may be spread out flat in water on a

slide, the water drained off, the tissue allowed to dry completely, and dammar added. This method is used to exhibit endothelium, and generally to stain intercellular substance. It depends upon the fact that the chlorides of the tissues are almost exclusively confined to the intercellular substance.

The following methods are especially useful in investigations relating to the nervous system :

21. *Marchi's solution.*—This is a mixture of Müller's fluid (2 parts) with 1 per cent. osmic acid (1 part). It is of value for staining nerve-fibres in the earlier stages of degeneration, before sclerosis sets in (especially a few days after the establishment of a lesion). All the degenerated medullated fibres are stained black, whilst the rest of the section remains almost unstained. It is best to put thin pieces of the brain or cord to be investigated singly into a large quantity of the solution (after previously hardening for ten days in Müller's fluid), and to leave them in it for a week or more ; if necessary sections can be stained ; in this case the process is more complicated.[1] In either case they are fixed on a slide and mounted by the usual process in xylol balsam or dammar.

22. *Weigert-Pal method.*—This method is chiefly used for the central nervous system. By it all medullated nerve-fibres are stained dark, while the grey matter and any sclerosed tracts of white matter are left uncoloured. The following modification of the original method can be recommended : Pieces which have been hardened in Müller's fluid and afterwards kept a short time in alcohol (without washing in water) are embedded in celloidin, and sections are cut as thin as possible. Or sections may be made by the freezing method direct from Müller's fluid, if the tissue is first soaked in gum-water for a few hours. In either case they are placed in water, and from this are transferred to Marchi's fluid (see above, § 21), in which they are left for a few hours. They are then again washed in water and transferred to Kulschitzky's hæmatoxylin (see above, § 3). In this they are left overnight, by which time they will be completely black. After again washing in water they are ready to be bleached. This is accomplished by Pal's method as follows: Place the overstained sections, first in $\frac{1}{4}$ per cent. solution of potassium permanganate for five minutes (or for a longer time in a weaker solution) ; rinse with water and transfer to Pal's solution (sulphite of soda 1 gramme, oxalic acid 1 gramme, distilled water 200 cubic centimetres), in which the actual bleaching takes place.[2] They are usually sufficiently differentiated in a few minutes : if not, they can be left longer in the solution without detriment. If after half an hour they are not differentiated enough, they must be put again (after washing) into the permanganate for some minutes, and then again into Pal's solution. After differentiation they are passed through water, alcohol (with or without eosin), and oil of bergamot (or xylol), to be mounted in xylol balsam or dammar. The advantages which this modification has over the original method are (1) even the finest medullated fibres are brought to view with

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[1] See Hamilton, *Brain*, 1897, p. 180.

[2] Diluted sulphurous acid solution may be employed instead of Pal's solution.

great surety; (2) the staining of the fibres is jet black, and offers a strong contrast to the colourless grey matter; (3) the sections are easily seen and lifted out of the acid hæmatoxylin, which has very little colour; (4) it is difficult to overbleach the sections; (5) the stain is remarkably permanent.

As a modification of the above, Bolton recommends to harden with formol, place the sections for a few minutes in 1 per cent. osmic acid, stain for two hours in Kulschitzky's hæmatoxylin at 40° C., and then proceed with the bleaching process.

23. *Staining with chloride of gold.*—α. *Cohnheim's method.*—Place the fresh tissue for from thirty to sixty minutes in a ½ per cent. solution of chloride of gold; then wash and transfer to a large quantity of water faintly acidulated with acetic acid. Keep for two or three days in the light in a warm place. This answers very well for the cornea. If it be principally desired to stain the nerve-fibrils within the epithelium, the cornea may be transferred after twenty-four hours (the outlines of the larger nerves should be just apparent to the naked eye) to a mixture of glycerine (1 part) and water (2 parts), and left in this for twenty-four hours more (Klein).

β. *Löwit's method.*—Place small pieces of the fresh tissue in a mixture of 1 part of formic acid to 2 to 4 parts of water for one-half to one minute; then in 1 per cent. chloride of gold solution for ten to fifteen minutes; then back again into the formic acid mixture for twenty-four hours, and into pure formic acid for twenty-four hours more. After removal from the gold, and whilst in the acid, the tissue must be kept in the dark. This method is especially good for motor nerve endings in skeletal muscle.

γ. *Ranvier's method.*—Immerse in lemon-juice for five to ten minutes, then wash with water and place in 1 per cent. gold-chloride solution for twenty minutes. Then treat either as in Cohnheim's or as in Löwit's method.

24. *Golgi's chromate of silver methods.*—These are chiefly employed for investigating the relations of cells and fibres in the central nervous system. Two methods are mostly used, as follows:

α. Very small pieces of the tissue which has been hardened for some weeks in 3 per cent. bichromate of potassium or Müller's fluid are placed for half an hour in the dark in 0·75 per cent. nitrate of silver solution, and are then transferred for twenty-four hours or more to a fresh quantity of the same solution (to which a trace of formic acid may be added). They may then be placed in 96 per cent. alcohol (half an hour), and sections, which need not be thin, are cut either from celloidin with a microtome or with the free hand after embedding (but not soaking) with paraffin. The sections are mounted in xylol balsam, which is allowed to dry on the slide: they must not be covered with a cover-glass, but the balsam must remain exposed to the air.

β. Instead of being slowly hardened in bichromate, the tissue is placed at once in very small pieces in a mixture of bichromate and osmic acid (3 parts of 3 per cent. bichromate of potassium or of Müller's fluid to 1 of osmic acid). In this it remains from one to eight days, a piece being transferred each day to 0·75 per cent. silver nitrate. The subsequent procedure is the same as described under *a*. For some organs it is found advantageous to repeat the process, replacing them for a day or two in the osmic-bichromate mixture after silver nitrate and then putting them back into silver nitrate (Cajal's double method). This method is not only more rapid than that in which bichromate of potassium alone is used, but is more sure in its results.

25. *Cox's chromate of mercury method.* This serves the same purpose as the Golgi methods. Mix 20 c.c. of 5 per cent. corrosive sublimate solution and 16 c.c. of 5 per cent. chromate of potassium solution with 30-40 c.c. distilled water, and add 20 c.c. of 5 per cent. bichromate of potassium solution to the mixture. Small pieces of fresh tissue are placed in this and left for two months or more. Sections of the tissues are then cut by the freezing microtome and placed either in 5 per cent. sodium carbonate solution or in dilute ammonia. They are then passed through water, grades of alcohol, and clove oil into dammar, and mounted without a cover-glass.

26. *Ehrlich's methylene-blue method.*—This method is one of great value for exhibiting nerve-terminations, and in some cases the relations of nerve-cells and fibres in the central nervous system. For its application the tissue must be living: it is therefore best applied by injecting a solution of methylene blue (1 part to 100 of warm saline solution) into a vein in an anæsthetised mammal, until the whole blood is of a bluish colour; or the injection may be made through the vessels of the part to be investigated, immediately after killing an animal. But fairly good results can also be obtained by immersing small pieces of freshly excised living tissue in a less concentrated solution (0·1 per cent.), or, in the case of the central nervous system, by dusting the methylene-blue powder over a freshly cut surface, allowing some time for it to penetrate, and then treating it with picrate of ammonia and Bethe's solution. In either case the tissue should be freely exposed to air; the blue colour then appears in the nerve-cells and axis-cylinders, even to their finest ramifications. It does not, however, remain, but after a time fades from them while other tissues become coloured. To fix the stain the tissue is taken at the moment that the nerve-fibres are most distinctly seen and is placed for an hour or two in saturated solution of picrate of ammonia, after which the preparation can be mounted in glycerine containing picrate of ammonia. But to allow of sections being made from it for mounting in balsam or dammar, it must, subsequently to the treatment with picrate of ammonia, be placed for some hours in Bethe's fluid, viz.:

Molybdate of ammonia, - - - -	1 gramme.
Chromic acid 2 per cent. solution, - - -	10 c.c.
Distilled water, - - - - - -	10 c.c.
Hydrochloric acid, - - - - -	1 drop.

This renders the colour insoluble in alcohol.

27. *Dogiel's modification of the Ehrlich method.*—Place the fresh tissue in a capsule containing 1 per 1000 methylene blue and keep at 36° C. for two hours.

Then place in 6 per cent. molybdate of ammonia for twenty-four hours; wash four hours in distilled water; dehydrate with alcohol, and pass through xylol into dammar or Canada balsam.

28. *Sihler's method of staining nerve-endings in muscle and blood-vessels.*—Macerate the tissue for eighteen hours in the following solution:

Ordinary acetic acid,	1 part.
Glycerine,	1 part.
1 per cent. chloral hydrate solution,	6 parts.

From this transfer to glycerine for from one to two hours; then unravel somewhat with needles and place for from three to ten days in the following:

Ehrlich's hæmatoxylin,	1 part.
Glycerine,	1 part.
1 per cent. chloral hydrate solution,	6 parts.

It may then be kept for any desired time in glycerine, which should be changed several times.

Preparations are made by careful dissociation with needles. If overstained they may be differentiated by acetic acid until the dark-blue colour is changed to violet. The muscle spindles and the end-plates are well shown by this method.

29. *Nissl's method of staining the chromatic granules in nerve-cells.*—This is a method of overstaining with methylene blue and subsequent differentiation with alcohol (see § 13). Nissl recommended 90 per cent. alcohol as the hardening agent, but both formol and corrosive sublimate followed by alcohol may be employed also. Toluidin blue (Mann) may be used in place of methylene blue. The sections may first be stained with 1 per cent. aqueous solution of eosin, and then, after rinsing in water, with 1 per cent. methylene-blue solution: they are best differentiated in aniline alcohol. The effect of heating the solutions to about 70° C. is to accelerate and accentuate the staining, which will then take only a few minutes.

A Nissl stain may also be obtained by placing thin pieces of the fixed and hardened nervous tissue in 1 per cent. solution of thionin for several days; after which the tissue is dehydrated and embedded in paraffin.

30. *Cajal's methods for exhibiting neurofibrils within nerve-cells and -fibres.*—*a.* A small piece of the tissue (brain, spinal cord, ganglion, etc.), not more than 4 mm. thick, and preferably from a young animal, is placed in 50 c.c. of rectified spirit to which 3 or 4 drops of ammonia may be added. After four to six hours in this, followed by twenty-four hours in absolute alcohol, rinse with distilled water and place in a large quantity of 1·5 per cent. solution of silver nitrate, which is maintained at a temperature of about 35° C. After being five or six days in this solution, the piece is removed, rinsed for a few seconds in distilled water, and transferred for twenty-four hours to the following solution:

Hydrokinone (or pyrogallic acid),	1 to 1·5 grammes.
Distilled water,	100 cub. cent.
Formol,	5 to 10 cub. cent.
Rectified spirit,	10 to 15 cub. cent.

The addition of alcohol to the above is not indispensable, but favours penetration. The piece is then washed in water for some minutes, transferred to alcohol, embedded in celloidin or paraffin, and sections are prepared and mounted in the ordinary way.

β. Place several small pieces of the fresh tissue direct in 2 per cent. silver nitrate solution at 35° C. in the dark : a piece is taken out on the third and on each subsequent day until the eighth. The piece is rinsed in distilled water for a minute or two and then immersed in the developing solution for twenty-four hours : after which proceed as above. The tissue should be placed on cotton wool in the silver solution. The central parts of the tissue are usually best, the superficial parts being often too dark.

31. *Bielchowsky's method for neurofibrils.*—Place small pieces in 12 per cent. formaline for twenty-four hours : wash in distilled water : transfer to 2 per cent. nitrate of silver for from three to five days : again wash in distilled water. Then transfer to the following solution, viz. : 2 per cent. nitrate of silver 20 c.c., to which three drops of a 40 per cent. solution of caustic potash are added, and enough ammonia to cause the disappearance of the precipitate produced. The pieces may be left in this solution for some hours or days. They are then transferred to 20 per cent. formaline solution for twenty-four hours. Sections may be cut by the freezing or paraffin methods. The sections can be toned on the slide with dilute gold chloride and afterwards fixed with hyposulphite of soda.

INDEX.

Achromatic spindle, 9, 18, 19.
— substance, 11.
Adenoid tissue, 92.
Adipose tissue, 80, 89.
Adrenals. *See* Suprarenal capsules.
Air-bubbles, 29.
Ameloblasts, 308.
Amitosis, 12.
Amœba, 3.
Amœboid movements, 3, 7, 8, 35, 36, 37, 43, 57.
Ansa lenticularis, 472, 498.
Aorta, 212.
Appendix, vermiform, 351.
Aqueduct, 458.
Arachnoid, 408, 499.
Archoplasm, 9, 393.
Arcuate fibres, 432, 434, 435, 466.
Areolar tissue, 80, 82.
— — cells of, 83.
— — fibres of, 82.
Arrector pili, 277.
Arteries, vessels and nerves of, 221.
— structure of, 208.
— variation in structure of, 212.
— and veins, smaller, structure of, 216.
Articular corpuscles, 191.
Association fibres, 486.
Attraction sphere, 18, 9, 13.
Auditory hairs, 536, 541.
— — meatus, 530.
Auerbach, plexus of, 336, 337.
Auriculo-ventricular bundle, 288.
Autonomic nerves, 153.
Axis-cylinder, 150, 152, 164, 183.
Axon, 158, 164, 183.

Bacteria, 29.
Baillarger, lines of, 485.
Basement membranes, 92.
Basilar membrane, 538, 539.
Basket-cells, 476.
Bechterew, nucleus of. *See* nucleus.
Bellini, ducts of, 369, 370.
Bethe's fluid, 560.
Bielchowsky's stain, 562.
Bile-canaliculi, 357.
Bile-ducts, 357.
Bladder, 376.
Blastoderm, 24.
Blood, 30.
Blood-cells, 38.
Blood-corpuscles, action of reagents upon, 48, 51.
— of amphibia, 52.
— coloured, 52, 33, 48.
— colourless, 33, 34, 51.
— — amœboid phenomena of, 57.
— — granules of, 35.
— — migration of, 59, 61, 221.
— — varieties of, 35, 36.
— development of, 38, 43, 46.
— enumeration of, 32.
— structure of, 33, 48.
Blood-crystals, 48, 51.
Blood-film, 30.
Blood-islands, 38.
Blood-platelets, 47, 30, 33, 37, 55, 221.
Blood-vessels, development of, 41, 222.
— structure of, 208, 216.
Bone, 81, 112.
— development of, 118, 125.
— lacunæ and canaliculi of, 114, 115, 117.
— lamellæ of, 114, 115, 116.
— marrow of, 43, 114.
Bowman, glands of, 530.
— membrane of, 505.
Brain, 428. *See* cerebrum, cerebellum, medulla oblongata, mesencephalon, pons.
— divisions of, 428.
— membranes of, 499.
Brain-sand, 473.
Bridging fibrils, 65, 145, 260.
Bronchi, 293.
Bronchial tubes, 293.
Bronchioles, respiratory, 293.
— terminal, 293.
Brownian movements, 29.
Bruch, membrane of, 511.
Brunner, glands of, 342.
Bundle. *See* tract.
Burdach, tract of, 413, 432.

Calleja, islands of, 452, 494.
Canaliculi, biliary, 357.
— of bone, 114.
— of nerve cells, 164.

Capillaries, 219, 221.
— circulation in, 221.
— lymphatic, 226.
Carnoy's fluid, 545.
Carotid gland, 254.
Cartilage, 81, 102.
— articular, 102, 103.
— calcified, 104.
— costal, 103, 108.
— development of, 106.
— embryonic, 106.
— fibro-, 103, 108, 111.
— hyaline, 103.
— ossification of, 118.
— parenchymatous, 106.
— transitional, 104.
— varieties of, 103.
Cartilage-bone, 118.
Cartilage-cells, 104.
— capsules of, 104, 105.
Cell, division of, 12.
— — amitotic, 12.
— — reduction, 17.
— embryonic, 1, 24.
— membrane of, 3, 9, 8.
— nucleus of, 3, 10, 13.
— structure of, 3.
Celloidin for embedding, 548.
Cell-plate, 19.
Cell-spaces, 2, 80, 83.
Cement of tooth, 300, 306.
Cement substance, 2, 63.
Central canal of cord, 409.
— fovea of retina, 524.
— tendon of diaphragm, 216.
Centriole, 9.
Centrosome, 8, 18, 19.
Cerebellum, 474.
— grey matter of, 475.
— peduncles of, 480.
— — superior, 457, 460, 468, 481.
— — inferior, 480.
— — middle, 446, 481.
Cerebrum, 474.
— basal ganglia of, 497.
— cortex of, 481.
— — structure of different parts, 487.
— peduncle of, 462.
Chemotaxis, 8.
Chondrin-balls, 106.
Choroid coat of eye, 501, 509.
Chromatic substance, 11.
Chromatolysis, 177.
Chromaffin or chromophil cells, 252, 254.
Chromomeres, 12.
Chromosomes, 12, 14, 17, 18.
Cilia, 72, 78.
— action of, 72, 78.
— — theories regarding, 78.
Ciliary muscle, 511.
Circulation, 217, 221.
Clarke, column of, 420.
Clasmatocytes, 84.
Claustrum, 403.
Clitoris, 378.
Coccygeal gland, 254.
Cochlea, 533, 538.
— canal of, 534, 539.
Cœlom, 231.
Cohnheim, areas of, 130.
— method of staining nerve-endings, 559.
Collagen, 83.
Collaterals, 166.
Colliculi, 462.
Colliculus, nervi optici, 516.
Colloid substance, 252, 258.
Colostrum-corpuscles, 282.
Columella, 538.
Commissural fibres, 486.
Commissures of cerebrum, anterior, 497.
— — posterior, 467.
— of spinal cord, 409.
Conjunctiva, 501.
Connective tissue, cells of, 80, 83.
— — development of, 98.
— — fibres of, 82, 83, 95, 96.
— — jelly-like, 92.
— tissues, 1, 80.
Corium, 264.
Cornea, 500, 504.
— nerve-endings in, 200, 509.
Corpora albicantia s. mamillaria, 471, 497.
— geniculata, 469.
— quadrigemina, 462.
Corpus cavernosum, 378.
— luteum, 400.
— spongiosum, 378.
— striatum, 497.
— subthalamicum, 472.
Corti, organ of, 533, 540.
— rods of, 540.
Cotton fibres, 29.
Cowper, glands of, 381.
Cox, mercuric-chromate method of, 560.
Crista acustica, 535.
Crus cerebri, 462.
Crusta, 462, 498.
— petrosa, 300, 306.
Cupula terminalis, 536.
Cutis vera, 259, 264.
Cytomitome, 8.
Cyton, 158.
Cytoplasm, 3, 8.

Decalcifying fluids, 547.
Decidua, 404.
Decussation of pyramids, 428.

Deiters, cells of, 543.
— nucleus of, 443, 444, 448.
Delafield's hæmatoxylin, 554.
Dendrons or dendrites, 158, 164, 183.
Dentine, 300, 309.
Descemet, membrane of, 507, 509.
Deutoplasm, 6.
Dilatator pupillæ, 512.
Division of cells, 12.
— of nucleus, 13, 17.
— reduction, 17, 21, 24.
— of ovum, 20.
Dobie, line of, 131.
Dogiel, method of, 560.
Doyère, eminence of, 205.
Dura mater, 408, 499.
Dust, 29.

Ear, external and middle, 530.
— internal, 533.
Ebner, glands of, 314.
Ehrlich, hæmatoxylin stain of, 554.
— methylene-blue method of, 560.
Elastic tissue, 81, 83, 94, 100, 111.
Eleïdin, 260, 264, 268.
Elementary particles, 33, 37.
Embedding, methods of, 547.
Embryonic cells, 1, 24.
Enamel, 300.
— formation of, 308.
— organ, 309.
End-bulbs, 156, 188, 189, 195.
Endocardium, 287.
Endomysium, 133.
Endoneurium, 156.
Endoplasm, 7.
Endothelium, 25, 68, 208, 218, 287.
— lymphatic, 225.
— serous, 230.
End-plates, 140, 205.
Ependyma, 425, 445.
Epicardium, 286.
Epidermis, 259.
Epididymis, 376, 382, 383.
Epineurium, 155.
Epiphysis cerebri, 472.
Epithelium, 63.
— ciliated, 64, 65, 72, 76.
— classification of, 64.
— columnar, 64, 72.
— germinal, 394.
— glandular, 64, 68.
— nerve-endings in, 199.
— pavement, 64, 68.
— protective, 65.
— respiratory, 296.
— secreting, 65.
— stratified, 64, 65.
— transitional, 65, 67, 378.
Epitrichial layer, 262.
Eponychium, 268.

Erectile tissue, 378.
Erythroblasts, 38, 41, 43, 48, 240.
Erythrocytes, 33, 42. *See also* blood-corpuscles, coloured.
Eustachian tube, 532.
Exoplasm, 7, 101.
Eye, 500, 503.
Eyelids, 500.
Eye-piece, 26.

Fallopian tubes, 394, 401.
Fascia dentata, 494.
Fasciculus retroflexus, 461, 471.
— solitarius, 438, 439.
Fat, 89. *See also* adipose tissue.
— absorption of, 344.
— in cartilage cells, 108.
Female pronucleus, 24.
Fenestrated membrane, 210.
Fibres. *See* connective tissue, muscle, nerve, etc.
Fibrin, 30, 37.
Fibro-cartilage, elastic, 103, 109.
— white, 103, 111.
Fibrous tissue, 81, 94, 96.
Fillet. *See* tract of fillet.
Fimbria, 492, 494.
Flechsig, method of, 413.
— tract of, 417, 435.
Flemming, fluid of, 546.
— germ-centres of, 235, 236, 245.
— stainable bodies of, 235, 245.
— method of staining nuclei, 557.
Forel, decussation of, 461 (footnote).
Formatio reticularis, 411, 432, 434, 435, 444, 460.
Freezing method for preparation of sections, 548.
Funiculus cuneatus, 411, 431.
— gracilis, 411, 431.

Gall-bladder, 358.
Ganglia, 158, 170.
— cells of, 170.
— development of, 185.
— spinal, 170, 185.
— sympathetic, 174, 185.
Ganglion of cochlea, 441.
— of glossopharyngeal, 438.
— of Scarpa, 441.
— of vagus, 437.
— Gasserian, 451.
— geniculate, 449.
— of habenula, 462, 470.
— interpeduncular, 462.
Gas-chamber, 73.
Genital corpuscles, 191.
Gennari, line of, 485.
Germinal spot, 396.
— vesicle, 396.
Giant cells of cerebrum, 483.

Giant cells of marrow, 45.
— — of spleen, 249.
Gianuzzi, crescents of, 323.
v. Gieson's stain, 555.
Gland or glands.
— agminated, 342, 339.
— anal, 351.
— of Bowman, 530.
— of Brunner, 342, 333.
— carotid, 254.
— ceruminous, 279, 530.
— classification of, 70.
— coccygeal, 254.
— of Cowper, 381.
— ductless, 70.
— of Ebner, 314.
— gastric, 328.
— hæmal, 232, 236.
— internally secreting, 71.
— lacrymal, 503.
— of Lieberkühn, 338.
— of Littré, 381.
— lymph, 225, 232.
— mammary, 282.
— Meibomian, 277, 502.
— Pacchionian, 499.
— pineal, 472.
— pituitary, 243, 256, 473.
— racemose, 70.
— saccular, 70.
— salivary, 319.
— sebaceous, 265, 277.
— secreting, 63, 68.
— serous, 314, 323.
— solitary, 241, 351.
— sweat, 265, 278.
— thymus, 232, 239.
— tubular, 70.
Glia cells, 181, 186.
Glisson, capsule of, 353.
Glomeruli of kidney, 364
— olfactory, 495.
Glycogen in colourless blood-corpuscles, 54.
— in liver cells, 356.
Goblet-cells, 76.
Gold-methods of staining nerve-endings, 559.
Golgi-Mazzoni corpuscles, 195.
Golgi, organs of, 195.
— cells of, 479.
— methods of preparing the nervous system, 559.
— reticulum of, 162.
— types of nerve-cells, 165.
Graafian follicles, 395.
Grandry, corpuscles of, 188, 192, 193.
Granules of protoplasm, 4.
— of colourless blood-corpuscles, 30, 35.
Ground-substance, 2, 82, 99, 101, 103, 112, 114, 145.
v. Gudden, method of, 179.
Gullet. *See* œsophagus.
Gustatory cells, 315.
— organs, 312.
— pore, 315.
Gyrus dentatus, 492, 494.
— hippocampi, 492.

Habenula, 470.
Hæmacytometer, 32.
Hæmal glands, 232, 236.
Hæmatin, 50.
Hæmatoblasts, 38.
Hæmatoidin, 51.
Hæmin, 51.
Hæmoglobin, 48, 51.
Hæmolysis, 49.
Hair-cells of internal ear, 536, 541, 543.
Hair-follicle, structure of, 268.
Hairs, 29, 265, 268.
— development of, 275.
— muscles of, 277.
Hardening solutions, 545.
Hassal, concentric corpuscles of, 240.
Haversian canals, 114, 117.
— fringes, 107.
— lamellæ, 115.
— systems, 115.
Hayem's solution, 32.
Heart, 284.
— muscle of, 141, 284.
— nerves of, 289.
— valves of, 289.
— vessels of, 289.
Heidenhain's stain, 554.
Henle, fenestrated membrane of, 210.
— looped tubules of, 368, 370.
— sheath of, 156, 192.
Hensen, line of, 131.
Hepatic lobules, 353.
— cells, 355.
Herbst, corpuscles of, 188, 193, 194.
Hippocampus major, 491, 493.
His, bundle of, 288.
Histogenesis, 24.
Histology, meaning of term, 1.
Hyaloid membrane, 527.
Hyaloplasm, 4, 10.
Hypophysis cerebri, 256, 473.
Hypothalamus, 472.

Idiozome, 393.
Intercellular channels, 65, 142, 260.
— substance, 2, 81, 82, 99, 101, 103, 112, 114, 145.
Internal capsule, 497, 498.
Intestine, large, 336, 350.
— small, 336.
Iris, 501, 511.

Jelly of Wharton, 101.
Jenner's stain, 556.

Karyokinesis, 12.
Karyomitome, 10.
Karyoplasm, 10.
Keratinisation, 64.
Kerato-hyaline, 260, 264.
Kidney, 364.
— blood-vessels of, 370.
— development of, 373.
Krause, membrane of, 131, 134.
Kultschitzky's hæmatoxylin stain, 554.
Kupffer, cells of, 355.

Labyrinth of ear, 533.
— of kidney, 370.
Lacrymal glands, 503.
Lacteals, 344.
Lacunæ of bone, 114, 115.
— of urethra, 381.
Lamellæ of bone, 114, 115, 116.
Lamina cribrosa, 504.
— fusca, 504.
— reticularis, 541.
— suprachoroidea, 511.
Landolt, fibre of, 519.
Langerhans, islets of, 359.
— centro-acinar cells of, 362.
Lanugo, 276.
Larynx, 293.
Lens, 525, 501.
Leucocytes, 33, 34, 46, 51, 57. (*See* also blood-corpuscles, colourless.)
Lieberkühn, crypts of, 338.
Ligamentum pectinatum, 507.
Ligula, 445.
Limbus of cochlea, 539.
Linen fibres, 29.
Linin, 12.
Lipoid substances, 3, 8, 33, 50.
Liver, 352.
— blood-vessels of, 353.
— cells of, 355.
— ducts of, 357.
— intracellular canals of, 355.
— lobules of, 353.
— lymphatics of, 358.
Löwit, chloride of gold method of, 559.
Lung, 290, 293.
— blood-vessels of, 298.
— development of, 299.
— lymph-vessels of, 299.
Luys, corpus subthalamicum of, 472.
Lymph-corpuscles. (*See* blood-corpuscles, colourless.)
Lymph-glands or lymphatic glands, 225, 232.
— — hæmal, 232, 236.
Lymph-plexuses, 228.
Lymph-vessels or lymphatics, 216, 225.
— connection with cells of connective tissue, 88, 228.
— development of, 229, 239.
— nerves of, 226.
Lymphocytes, 35, 36, 43.
Lymphoid nodules, 232, 233, 236, 341, 351.
Lymphoid tissue, 81, 92, 233, 239.
— — development of, 239.

Macula acustica, 536.
— lutea of retina, 524.
Male pronucleus, 24.
Mallory, stain of, 557.
Malpighi, rete mucosum of, 260.
— pyramids of, 364.
Malpighian corpuscles of kidney, 364.
— — of spleen, 239, 244.
Mammary glands, 282.
Marcano's solution, 32.
Marchi's method of staining degenerated nerve-fibres, 558.
Marrow, 43, 114, 118.
Martinotti, cells of, 485.
Mast-cells, 84.
Mayer's stain, 554, 555.
Measuring objects, 27.
Medulla oblongata, 428.
— — nerves arising from, 435.
Megakaryocytes, 45.
Meissner, plexus of, 336, 338.
Membrana tectoria, 544.
— tympani, 532.
Mesencephalon, 428, 446, 458.
Mesenchyme, 25, 98.
Mesothelium, 25, 68.
Metencephalon, 428.
Methods of embedding, 547.
— of measuring microscopic objects, 27.
— of mounting sections, 545, 552.
— of preparing sections, 548.
— of preserving and hardening, 545.
— of staining, 553.
Meynert, bundle of. *See* tracts.
— decussation of, 461.
Micron, 34.
Micrometer, 27.
Microscope, 26.
Microscopic work, requisites for, 26.
Microtomes, 548.
Mid-brain, 428, 458.
Migration of colourless blood-corpuscles, 59, 61, 221.
Minot, microtome of, 550.
Mitochondria, 5, 362, 393.

Mitosis, 12.
— heterotypical, 17, 20.
— homotypical, 17, 20.
— multipolar, 19.
— somatic, 17.
Moist chamber, 73.
Mould, 29.
Mounting fluids, 545, 552.
Mouth, mucous membrane of, 316.
Mucigen, 76, 321.
Mucous cells, 323.
Mucus-secreting cells, 76, 321.
Muir's stain, 556.
Müller, fibres of, 522.
— helicine arteries of, 378.
— muscle of, 511.
— fluid of, 545.
Muscle, blood-vessels and lymphatics of, 138, 139.
— cardiac, 138, 141.
— changes in contraction, 135, 137.
— corpuscles, 131.
— development of, 140.
— ending of, in tendon, 138.
— involuntary or plain, 138, 144.
— — development of, 147.
— — of arteries, 210.
— nerves of, 140, 202.
— nuclei of, 131, 142.
— of insects, 133, 134.
— in polarized light, 136.
Muscle, principal disk of, 135.
— red, 133.
— spindles, 128, 140, 188, 202.
— structure of, compared with protoplasm, 137.
— voluntary or cross-striated, 128, 129.
Muscle-plate, 140.
Myelencephalon, 428.
Myelin, 151.
Myelination, 413.
Myelocytes, 43.
Myeloplaxes, 45.
Myocardium, 284.

Nails, 265.
— development of, 267.
Nerve or nerves.
— abducent, 450.
— autonomic, 153.
— chorda tympani, 449
— cochlear, 441, 544.
— eighth, 440, 534.
— facial, 448.
— glossopharyngeal, 438.
— hypoglossal, 436.
— motor, 183.
— optic, 466.
— spinal accessory, 437.
— trigeminal, 431, 450.
Nerve or nerves.
— vagus, 437.
— vestibular, 443.
— of Wrisberg, 448.
Nerve-cells, 157.
— bipolar, 165.
— degeneration of, 177.
— development of, 183.
— multipolar, 165.
— processes of, 164.
— reticulum of, 162.
— of spinal ganglia, 170.
— of sympathetic ganglia, 174.
— trophospongium of, 164.
— types of, 166.
— unipolar, 164, 170.
Nerve-fibres, 140.
— axis cylinder of, 150, 152, 164.
— degeneration of, 177.
— development of, 183.
— medullated, 148.
— medullary segments of, 151.
— motor, terminations of, 188, 205.
— non-medullated, 148, 153.
— regeneration of, 179.
— sensory, modes of termination of, 188, 189, 199, 202.
— size of, 152.
— sheaths of, 149, 156, 185.
— varieties of, 148.
Nerve-trunks, structure of, 154.
Nerve-unit, 167.
Nervi nervorum, 156.
Neuroblasts, 183.
Neurofibrils, 152, 158, 161, 179.
Neuroglia, 181, 186, 411, 479, 487.
Neurokeratin, 151.
Neurolemma, 150, 185.
Neurone, 158, 167, 469.
— theory, 170.
Neuro-synapse, 170.
Nissl, granules of, in nerve-cells, 158.
— degeneration, 177.
— method of staining nerve-cells, 561.
Nuclein, 11.
Nucleolus, 11, 14.
Nucleus of cell, 3, 8, 10, 13.
Nucleus or nuclei (nerve).
— of abducens, 450.
— of accessory, 432, 437.
— accessory auditory, 441.
— ambiguus, 437.
— of Bechterew, 443, 444.
— caudatus, 497.
— of cochlear nerve, 441.
— commissural, 438.
— cuneatus, 414, 431.
— — outer, 444.
— of Deiters, 443, 444, 448.

Nucleus or nuclei.
— dentatus, 435, 474.
— descending, of facial, vagus, and glossopharyngeal, 438, 440.
— descending vestibular, 443.
— of facial, 448.
— of fasciculus teres, 437.
— of fillet, 461.
— of glossopharyngeal, 433, 438.
— gracilis, 413, 431.
— of hypoglossal, 433, 436, 440.
— lateral, 429.
— lenticularis, 497, 498.
— oculomotor, 458.
— of olive, 429, 435, 444.
— of pons, 446.
— of posterior longitudinal bundle, 460.
— preolivary, 448.
— red, of tegumentum, 460.
— semilunar, 448.
— of Stilling, 420, 474.
— superior olivary, 442, 448.
— tecti (s. fastigii), 474.
— of thalamus, 467.
— of trapezium, 447.
— of trigeminal, 434, 450.
— trochlear, 459.
— of vagus, 432, 433, 437.
— of vestibular nerve, 434, 443.

Odontoblasts, 305, 309.
Œsophagus, 316.
Olfactory bulb, 491, 494.
— cells, 529.
— glomeruli, 495.
— mucous membrane, 528.
— nerve-fibres, 495.
— path, 497.
— tract, 491, 494.
Olive, 429, 432, 435.
— superior, 442, 448.
Omentum, 216.
Onychogenic substance, 267.
Oocytes, 396.
Oogenesis, 397.
Opsonins, 61.
Optic chiasma, 466.
— nerves, 466.
— thalamus, 467, 497.
— tract, 465, 466, 470.
Ora serrata, 525.
Ossification, intracartilaginous, 118.
— intramembranous, 118, 125, 127.
Osteoblasts, 118, 119, 127.
Osteoclasts, 122, 311.
Osteogenic fibres, 125.
Otoliths, 536.
Ovary, 394.
Ovum, 24, 394, 395.
— division of, 20.

Pacinian corpuscles, 188, 189, 192, 221, 265, 267, 363, 378.
Pancreas, 353, 359.
Papillæ of hairs, 268.
— of tongue, 312.
— of skin, 264.
— of kidney, 364.
Paranucleus, 5, 362.
Paraplasm, 6.
Parathyroids, 253.
Pelvis of kidney, 364.
Penis, 376, 378.
Perforating fibres, 116.
Pericardium, 286.
Penineurim, 155.
Periosteum, 114, 117.
Perimysium, 139.
Pes pedunculi, 462.
Peyer, patches of, 239, 342.
Phagocytes, 35, 36, 37, 61, 236, 249, 355.
Pharynx, 316.
Phototaxis, 8,
Pia mater, 408, 499.
Pick, bundle of, 430.
Pigment-cells, 85.
Pigment-granules, 161.
Pineal gland, 472.
Pinna, 530.
Pituitary body, 243, 256, 473.
Placenta, 394, 404.
Plasma cells, 85.
Pleura, 299.
Polar bodies, 21.
Pons, 446.
— nerves arising from, 448.
Portal canal, 353.
Preserving solutions, 545.
Prickle-cells, 65.
Projection fibres, 486.
Pronuclei, 24.
Proprio-spinal fibres of cord, 414, 419.
Prostate, 376, 381.
Protoplasm, 3.
Pseudonucleoli, 11.
Pseudopodia, 59.
Purkinje, cells of, 475.
— fibres of, 284, 288.
Pyramids of medulla oblongata, 428, 429, 446.

Ranvier, gold-chloride method of, 559.
— constrictions of, 151.
— picro-carmine stain of, 555.
v. Recklinghausen, method of stainin with silver nitrate, 557.
Reil, fillet of, 442, 455.
— island of, 483.
Reissner, membrane of, 539.
Remak, fibres of, 154.

Restiform body, 480.
Reticular or retiform tissue, 80, 91, 353, 433, 440, 444.
Retina, 501, 514.
— macula lutea of, 524.
— pars ciliaris of, 525.
— sensory epithelium of, 520.
Rhinencephalon, 491.
Ringer's solution, 30.
Rolando, tubercle of, 431.
Rollett's method of staining muscle, 128.
Rouleaux of blood-corpuscles, 30, 33, 34, 50.
Ruffini, organs of, 195.

Saccule, 534, 535.
Salivary corpuscles, 63, 236.
— glands, 319
Sarcolemma, 128, 129, 141, 144.
Sarcomeres, 134.
Sarcoplasm, 130.
Sarcostyles, 129, 130.
Sarcous elements, 129, 134.
Schwann, sheath of, 150.
Sclerotic coat of eye, 503.
Sections, preparation of, 548.
Semicircular canals, 533, 535.
Seminiferous tubules, 386.
Serous membranes, 216, 225, 230.
Sertoli, cells of, 387.
Sharpey, fibres of, 116.
Sihler's method of staining nerve-endings, 561.
Siliqua olivæ, 435.
Silver-methods, 559, 562.
Sinusoids, 209, 220, 223, 251, 254, 355.
Skin, 259.
Spermatogenesis, 390.
Spermatozoa, 376, 388.
Sphincter ani, internal, 351.
— pupillæ, 511.
Spinal bulb. *See* medulla oblongata.
Spinal cord, 408.
— — blood-vessels of, 425.
— — cell columns of, 420, 423.
— — central canal of, 409, 425, 432.
— — characters in different parts, 411.
— — commissures of, 409.
— — connection of nerve-roots with, 424, 409.
— — cornua of, 409, 411, 423, 428, 431.
— — grey matter of, 409, 411, 420.
— — membranes of, 408.
— — nerve-cells of, 420.
— — proprio-spinal fibres of, 414, 419.
— — tracts in, 408, 413.
— — white columns of, 409, 411, 413, 431.
Spinal ganglia, 170.
Spindle, achromatic, 9, 18, 19.
Spleen, 243.
Splenic cells, 61, 249.
— lobules, 249.
Spongioblasts, 181, 186.
Spongioplasm, 4, 7.
Staining of sections, 553.
Stanley-Kent, bundle of, 288.
Starch granules, 27.
Stilling, nucleus of, 420.
Stomach, 326.
— blood-vessels of, 333.
— glands of, 328.
— lymphatics of, 333.
Stomata, 216, 231.
Stria medullaris, 470.
— vascularis, 543.
Stroma (of blood-corpuscle), 33, 48, 50.
Substantia gelatinosa, 411, 451.
— nigra, 402.
Subthalamus, 472.
Suprarenal capsules, 243, 249.
Sweat-glands, 265, 278.
Sympathetic ganglia, 174.
— nerves, 153.
Synapse, 18, 167, 170.
Syncytium, 2, 142, 147, 223, 365.
Synovial membranes, 102, 106.

Tactile corpuscles, 189.
— disks, 192, 201.
Tænia, 445, 446.
Taste-buds, 314.
Teeth, 300.
— formation of, 306.
— pulp of, 305.
Tegmentum, 456, 460, 472.
Telencephalon, 428.
Tendon, 97.
— connection with muscle, 138.
— nerve-endings in, 195.
Tendon-cells, 97.
Testicle, 376, 382.
— intertubular tissue of, 386.
Tetrads, 17.
Thalamencephalon, 428, 446, 467.
Thalamus, 467, 497.
Thermotaxis, 8.
Thrombocytes, 37, 52.
Thymus gland, 232, 239.
Thyroid body, 243, 252.
Tissues, enumeration of, 1.
— formation from blastodermic layers, 24.
Tongue, 312.
Tonsils, 232, 236.
Tooth. *See* teeth.
Trachea, 290.
Tract or tracts, methods of studying, 408.

Tract or tracts or bundles.
— anterior (ventral) longitudinal. *See* tecto-spinal tract.
— anterolateral ascending. *See* tract of Gowers.
— — descending. *See* tracts of Loewenthal.
— ascending, 413, 414, 416, 417, 453.
— bulbo-thalamic. *See* tract of fillet.
— of Burdach, 413, 432.
— central acoustic, 461.
— — of cranial nerves, 456, 468, 470.
— — of tegmentum, 435, 452.
— cerebello-bulbar, 440.
— comma, 414.
— of cord, 413.
— cortico-bulbar, 452, 456.
— cortico-pontine, 446, 462.
— cortico-spinal. *See* pyramid tract.
— crossed pyramidal. *See* pyramid tract.
— descending, 413, 414, 416, 417, 452, 456.
— descending cerebellar, 417.
— direct pyramid. *See* pyramid tract.
— myelination of, 413.
— of fillet, 432, 434, 442, 453, 461, 468.
— of Flechsig, 417, 435.
— of Goll, 413, 432.
— of Gowers, 419, 435, 458.
— of Gudden, 461 (footnote), 471.
— of Helweg, 417.
— of Lissauer, 419.
— of Loewenthal, 417, 444.
— of Marie, 420.
— of Meynert, 461, 462, 466, 471.
— of Monakow, 417, 452, 460.
— of Münser, 461.
— of Pick, 430.
— olfactory, 494.
— olivo-cerebellar, 435.
— olivo-spinal. *See* tract of Helweg.
— optic, 464, 465, 466, 468.
— ponto-spinal, 417, 452.
— posterior (dorsal), longitudinal, 417, 434, 444, 448, 452, 460.
— prepyramidal. *See* tract of Monakow.
— pyramid, 416, 428, 430, 446, 452, 462, 499.
— of Risien-Russell, 481.
— rubro-spinal. *See* tract of Monakow.
— spino-cerebellar, 417, 419, 435, 458, 480.
— spino-tectal, 419.
— spino-thalamic, 419, 468.
— sulco-marginal, 420.
Tract or tracts or bundles.
— tecto-spinal, 417, 434, 453, 461, 466.
— thalamo-bulbar, 456.
— thalamo-olivary, 435, 453.
— transverse peduncular, 467.
— ventral longitudinal. *See* tecto-spinal tract.
— vestibulo-motor. *See* posterior longitudinal tract.
— vestibulo-spinal, 452.
— of vicq d'Azyr, 471.
Trapezium, 441, 442, 447.
Trophospongium, 4, 164.
Tubercle of Rolando, 431.
Tuberculum acusticum, 441.
— olfactorium, 494.
Tympanum, 530.

Ureter, 376.
Urethra, 376, 380.
Urinary bladder, 376.
Uriniferous tubules, 364, 366, 370, 373.
Uterus, 394, 402.
Utricle, 534, 535.

Vagina, 394.
Vas deferens, 382, 384.
Vasa vasorum, 221.
Vasoformative cells, 42, 223.
Veins, structure of, 208, 213, 216.
— valves of, 215.
— variations in, 215.
Ventricle, fourth, 432, 444, 456.
Vermiform appendix, 351.
Vesiculæ seminales, 385.
Villi, arachnoidal, 499.
— fœtal, 404.
— of intestine, 342.
— of synovial membrane, 107.
Vitellus, 309.
Vitreous humour, 527.
Volkmann, canals of, 116.

Wallerian degeneration, 1 7, 413.
Wander cells, 85.
Warming apparatus, 57.
Weigert-Pal method for staining sections of the nervous system, 558.
Wharton, jelly of, 101.
Williams, microtome of, 549.
Woollen fibres, 29.
Wrisberg, nerve of, 448, 449.

Yeast, 29.

Zenker, fluid of, 545.
Zinn, zonule of, 527.
Zymogen, 324.

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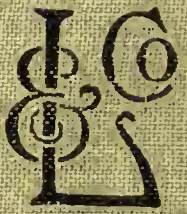
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